Malonate Anion Induced Favorskii-Type Rearrangement. 2.[1] Reaction of Acyclic α-Halo Ketones with Carbanions Leading to Cyclopropanols[2]

Takashi Sakai, Tsuyoshi Katayama, and Akira Takeda*

Department of Synthetic Chemistry, School of Engineering, Okayama University, Tsushima, Okayama 700, Japan

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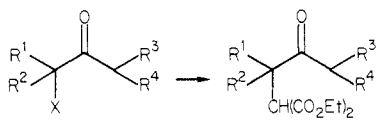
The reaction of 3-bromo-3-methyl-2-butanone (**6a**) with ethyl sodiomalonate (**2**) in refluxing THF gave 1-[bis(ethoxycarbonyl)methyl]-2,2-dimethylcyclopropanol (**9a**), the Favorskii-type intermediate, in 51% yield. Similar reactions of acyclic halo ketones such as 2-bromo-2-methyl-3-pentanone (**6b**), 1-acetyl-1-bromocyclohexane (**6c**), and 1-acetyl-1-bromocyclopentane (**6d**) with **2** also gave the corresponding cyclopropanols **9b–d** in 42–56% yields. On the contrary, the α-halo ketones (**6f–l**) possessing a primary or secondary carbon atom at the α position afforded the S_N2 products **10f–l**. The behavior of 3-chloro-3-methyl-2-butanone (**6e**) was quite different from that of its bromo homologue **6a**, giving a mixture (16:45:39) of **9a**, 1,1-bis[bis(ethoxycarbonyl)methyl]-2,2-dimethylcyclopropane (**14**), and 1-[bis(ethoxycarbonyl)methyl]-2,2-dimethyl-1-[(ethoxycarbonyl)methyl]cyclopropane (**15**) in 75% total yield. Hydrolysis of **9a** with 0.2 N NaOH at room temperature gave the acid ester **18**, which afforded a mixture of 3-carboxy-4,5,5-trimethyl-2(5*H*)-furanone (**22a**, 27% yield) and its ethyl ester (**22b**, 39% yield) on heating. When the hydrolysis was carried out in 2 N NaOH at 10 °C, **9a** gave 1-(dicarboxymethyl)-2,2-dimethylcyclopropanol (**23**, 60% yield) together with **22a** (27% yield). Similar hydrolysis of **9a** at 30 °C afforded 4,4-dimethyl-3-oxopentanoic acid (**24**, 38% yield) and 3,3-dimethyl-2-butanone (**25**, 18% yield). The bromination of **9a** with Br_2 caused the ring opening to give ethyl 5-bromo-4,4-dimethyl-2-(ethoxycarbonyl)-3-oxopentanoate (**30**) in 76% yield. The ester **30** was cyclized to the oxetane **31** in 77% yield.

Several interesting attempts have been made to isolate cyclopropanone or cyclopropanol intermediates in the course of mechanistic studies of the Favorskii rearrangement. In 1962, Fort[3] reported the capture of a cyclopropanone intermediate in the reaction of α-chlorodibenzyl ketone with 2,6-lutidine as the Diels–Alder adduct of furan. In 1965, Turro[4] further substantiated the mechanism by demonstrating that the alternatively prepared cyclopropanone readily underwent a cleavage to give the Favorskii product in the presence of sodium methoxide. Pazos,[5] in 1967, reported the first isolation of the cyclopropanone intermediate, i.e., *trans*-2,3-di-*tert*-butylcyclopropanone, with sterically hindered base. In the previous paper,[1] we reported the isolation of 6-[bis(ethoxycarbonyl)methyl]bicyclo[3.1.0]hexan-6-ol (**3**), the Favorskii-type intermediate in the reaction of 2-chlorocyclohexanone (**1**) with ethyl sodiomalonate (**2**). The cyclopropanol **3** was successfully converted into β-keto ester **4** or ketone **5** as a result of ring contraction. The present reaction not only represents the first example of the carbanion-induced Favorskii-type rearrangement but also will provide new synthetic procedures to obtain a variety of cyclopropanols, β-keto esters and ketones. As an extension of the previous work, we further investigated the reaction of various acyclic α-halo ketones **6** with malonate and/or carbanions other than malonate and found that there exists a definite relationship between the reactivity and the class of the carbon atom bearing halogen. Among acyclic ketones so far investigated, only dialkylhalomethyl ketones, with a few exceptions,[6] gave the corresponding cyclopropanols **9** and **16**. Both halomethyl ketones and alkylhalomethyl ketones underwent a substitution to give γ-ketonic esters **10** (Table I), whose boiling points and spectral data have been tabulated in Table IV. The alkaline hydrolysis of cyclopropanol **9a** was also studied. This paper describes the results of these experiments and

Table I



6 **10**

compd	substituents	S_N2 product	yield,[a] %
6f	$R^1 = R^2 = H$, $R^3 = R^4 = Me$, X = Br	10f	81
6g	$R^1 = R^2 = R^3 = R^4 = H$, X = Cl	10g	14
6h	$R^1 = R^2 = R^3 = R^4 = H$, X = Br	10g	75
6i	$R^1 = R^2 = R^3 = H$, $R^4 = Me$, X = Br	10i	94
6j	$R^1 = Me$, $R^2 = R^3 = R^4 = H$, X = Cl	10j	19
6k	$R^1 = Me$, $R^2 = R^3 = R^4 = H$, X = Br	10j	43
6l	$R^1 = i\text{-Pr}$, $R^2 = R^3 = R^4 = H$, X = Br	10l	25
6m[10]	$R^1 = R^2 = Me$, $R^3 = H$, $R^4 = CO_2Et$, X = Br	10m	15
6n[10]	$R^1 = Me$, $R^2 = CO_2Et$, $R^3 = R^4 = H$, X = Cl	10m	3

[a] Procedure A (in THF, at room temperature).

(1) Part 1 of this series: Sakai, T.; Amano, E.; Kawabata, A.; Takeda, A. *J. Org. Chem.* **1980**, *45*, 43.

(2) A part of the present work was presented at the 40th Annual Meeting of the Chemical Society of Japan, Fukuoka, Oct 1979.

(3) Fort, W. *J. Am. Chem. Soc.* **1962**, *84*, 4979.

(4) Turro, N. J.; Hammond, W. B. *J. Am. Chem. Soc.* **1965**, *87*, 3258.

(5) Pazos, J. F.; Greene, F. D. *J. Am. Chem. Soc.* **1967**, *89*, 1030. Pazos, J. F.; Pacifici, J. G.; Pierson, G. O.; Sclove, D. B.; Green, F. D. *J. Org. Chem.* **1974**, *39*, 1990.

(6) 2-Chloro-2,4-dimethylpentan-3-one (**6o**) was unreactive. 1-Bromocyclopropyl methyl ketone (**6p**) afforded uncharacterizable, complex material.

0022-3263/81/1946-2924$01.25/0

Table II. Cyclopropanols 9a-d and 16

compd[a,h]	yield, %	IR, cm^{-1} OH	IR, cm^{-1} C=O	^1H NMR, δ	MS, m/e[b]
9a	51[c]	3450	1730	[d]0.47 (d, 1 H, J = 6 Hz, ring H), 0.63 (d, 1 H, J = 6 Hz, ring H), 1.10 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 1.34 (t, 6 H, J = 7 Hz, ester 2 CH_3), 3.13 (s, 1 H, α-CH of ester), 3.48 (br s, 1 H, OH), 4.28 (q, 4 H, J = 7 Hz, ester 2 CH_2)	244 (M^+, 0.3), 226 (M − H_2O, 1), 171 (M − CO_2Et, 7), 160 ($CH_2(CO_2Et)_2$, 48)
9b	42[e,f]	3560	1740	[g]0.44-0.67 (m, 1 H, ring H), 1.01 (d, 3 H, J = 6 Hz, CH_3), 1.02 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3), 1.29 (t, 6 H, J = 7 Hz, ester 2 CH_3), 3.21 (s, 1 H, α-CH of ester), 3.30 (br s, 1 H, OH), 4.26 (q, 4 H, J = 7 Hz, ester 2 CH_2)	248 (M^+, 0.3), 240 (M − H_2O, 0.2), 213 (M − OEt, 2), 187 (12), 160 ($CH_2(CO_2Et)_2$, 56), 115 (59), 29 (100)
9c	53[c,f]	3540	1735	[d]0.40 (d, 1 H, J = 6 Hz, C_2H), 0.55 (d, 1 H, J = 6 Hz, C_2H), 1.30 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.52 (m, 10 H, 5 CH_2), 3.12 (s, 1 H, α-CH of ester), 3.49 (br s, 1 H, OH), 4.21 (q, 4 H, J = 7 Hz, ester 2 CH_2)	
9d	56[c,f]	3530	1730	[d]0.62 (d, 1 H, J = 6 Hz, C_2H), 0.78 (d, 1 H, J = 6 Hz, C_2H), 1.24 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.64 (m, 8 H, 4 CH_2), 3.09 (s, 1 H, α-CH of ester), 3.50 (br s, 1 H, OH), 4.22 (q, 4 H, J = 7 Hz, ester 2 CH_2)	270 (M^+, 0.08), 252 (M − H_2O, 0.05), 197 (M − CO_2Et, 6), 160 ($CH_2(CO_2Et)_2$, 57), 133 (37), 115 (51), 87 (42), 69 (44), 29 (100)
16	39[c,f]	3530	1735	[g]0.33-0.67 (m, 2 H, ring 2 H), 0.96 (s, 1.1 H), 1.01 (s, 1.9 H), 1.14 (s, 1.9 H), 1.20 (s, 1.1 H), 1.27 (t, 1.1 H, J = 7 Hz), 1.29 (t, 1.9 H, J = 7 Hz), 3.40 (br s, 1 H, OH), 3.86 (s, 0.63 H), 3.91 (s, 0.37 H), 4.24 (q, 1.5 H, J = 7 Hz), 4.28 (q, 2.5 H, J = 7 Hz), 7.4-7.7 and 7.9-8.1 (m, 5 H, C_6H_5)	294 (M − H_2O, 2), 171 (M − $SO_2C_6H_5$, 7), 77 (C_6H_5, 100)

[a] Obtained as an oil. [b] Relative intensity in parentheses. [c] Procedure A (in THF, under reflux). [d] CCl_4. [e] Procedure A (in THF, room temperature). [f] Isolation by column chromatography on silica gel (benzene–MeOH, 40:1). [g] $CDCl_3$. [h] Compound 9d was not stable enough to get acceptable elemental analysis; satisfactory analytical data (±0.4% for C, H) were reported for all other compounds.

discusses the mechanism of the reaction.

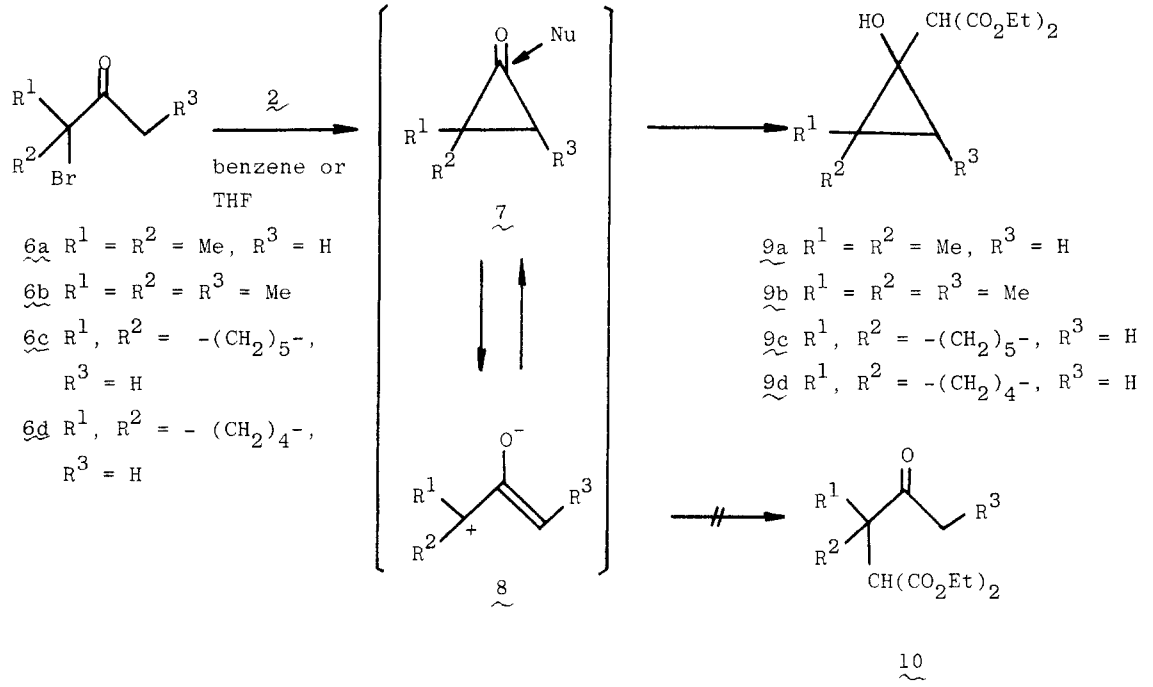
The reaction of 3-bromo-3-methyl-2-butanone (**6a**) with an equivalent amount of ethyl sodiomalonate (**2**) in refluxing THF gave 1-[bis(ethoxycarbonyl)methyl]-2,2-dimethylcyclopropanol (**9a**) in 51% yield (Scheme I) as might be expected from the behavior of **1** toward **2**.[1] The yield of **9a** was improved up to 61% when a 1-equiv excess of **2** was used. The cyclopropanol structure of **9a** has been unequivocally elucidated by spectroscopic methods and by analysis. Its IR spectrum showed a sharp absorption at 3450 cm^{-1} (OH), and the ^1H NMR spectrum exhibited two doublets at δ 0.47 (1 H, J = 6 Hz) and 0.63 (1 H, J = 6 Hz), indicating the presence of two geminal ring protons (Table II). Both the molecular ion peak at m/e 244 and the ^{13}C NMR (Table III) firmly supported its structure. The reaction of **6a** with **2** in refluxing benzene likewise afforded the cyclopropanol **9a** in a 64% yield together with a very small amount (2% yield) of 3-(ethoxycarbonyl)-4,5,5-trimethyl-2(5*H*)-furanone (**22b**).[7] The behavior of **6a** here forms a marked contrast to that of the cyclic halo ketone **1**, which is known to give solely ethyl *C*-(2-oxocyclohexyl)malonate (**11**) in the appropriate reaction. The above difference of the reactivity in the refluxing benzene found between the halo ketones **1** and **6a** is probably attributable to the difference in the stabilities of the produced cyclopropanols, since the compound **3** is readily transformed to **11** in refluxing benzene in the presence of 0.05 equiv of NaH, while compound **9a** remains intact under the same reaction conditions. Similar reactions of acyclic dialkylbromomethyl ketones such as 2-bromo-2-methyl-3-pentanone (**6b**), 1-acetyl-1-bromocyclohexane (**6c**), and 1-acetyl-1-bromocyclopentane (**6d**) with **2** also gave the corresponding cyclopropanols (**9b–d**) in 42–56% yields.

In THF, the chloro homologue (**6e**) of **6a** reacted with 2 equiv of **2** to give a 16:45:39 mixture of **9a**, 1,1-bis[bis(ethoxycarbonyl)methyl]-2,2-dimethylcyclopropane (**14**), and 1-[bis(ethoxycarbonyl)methyl]-2,2-dimethyl-1-[(ethoxycarbonyl)methyl]cyclopropane (**15**) in a 75% total yield (Scheme II). The discrepancy in obtainable products between **6a** and **6e** can be explained by the assumption that in the reaction of the less reactive chloro ketone **6e**, the initial product **9a** tends to be subjected to the prevalent attack of **2**, which is still predominantly present in the reaction mixture, thus affording **14** and **15** secondarily, while the bromo ketone **6a** uses up **2** more immediately to minimize the formation of byproducts. Although two paths can be postulated for the formation of compounds **14** and **15** as shown in Scheme II, path B appears unacceptable because the reaction of **2** with compound **12**, which was alternatively prepared by $TiCl_4$-catalyzed condensation[8] of **6e** and ethyl malonate, failed to give either

(7) Pavlova, L. A.; Belogorodskii, V. V.; Venus-Danilova, E. D. *Zh. Obshch. Khim.* **1966**, *36*, 1386. The IR and ^1H NMR spectra of **22b** were identical with those of an authentic sample.

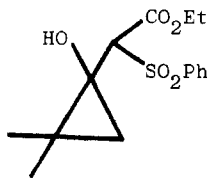
(8) Lehnert, W. *Tetrahedron* **1973**, *29*, 635.

Scheme I

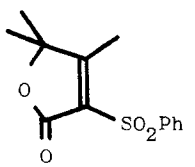


of these compounds in an appreciable amount. Path A, on the other hand, has been substantiated by the fact that **9a** reacted with 1 equiv of **2** in refluxing THF to give a 60:22:18 mixture of **9a**, **14**, and **15**.

The reaction of **6a** with sodium salt of ethyl (benzenesulfonyl)acetate[9] analogously gave the corresponding cyclopropanol (**16**) in 39% yield in addition to a minor



16



17

product of 3-(benzenesulfonyl)-4,5,5-trimethyl-2(5*H*)-furanone (**17**, 9% yield). On the contrary, halomethyl ketones (**6f–i**), alkylhalomethyl ketones (**6j–l**), and halogenated β-keto esters (**6m** and **6n**), which are listed in Table I, only afforded the substitution products **10f–n**.

The chemical properties of **9a** were then investigated. Hydrolysis of **9a** with 0.2 N NaOH at room temperature gave the acid ester **18** in 70% yield. On being heated at 200 °C, the acid ester **18** underwent a thermal rearrangement to afford 3-carboxy-4,5,5-trimethyl-2(5*H*)-furanone (**22a**,[7] 27% yield) and its ethyl ester (**22b**, 39% yield). A possible mechanism of the reaction is illustrated in Scheme III. It may be suggested that the thermal treatment of **18** would first cause dehydration to furnish the unsaturated acid ester **19**, which is subsequently transformed to the products via its ionic counterpart, i.e., the resonance-stabilized zwitterion **20**. Upon thermal treatment **9a** underwent similar skeletal rearrangement to the furanone **22b** in 46% yield.

Hydrolysis of **9a** with 2 N NaOH at 10 °C gave the crystalline dicarboxylic acid **23** (60% yield) together with 2(5*H*)-furanone **22a** (27% yield). The hydrolysis of **9a** with 2 N NaOH carried out at 30 °C, however, gave only 4,4-dimethyl-3-oxopentanoic acid (**24**)[11] and 3,3-dimethyl-2-butanone (**25**) in 38% and 18% yields, respectively. The similar treatment of spiro compound **9c** also afforded 1-acetyl-1-methylcyclohexane (**26**)[12] in 51% yield. These facts strongly suggest that increasing basicity and temperature of the reaction media favor the ring opening in a Favorskii fasion. When **9a** is warmed with NaH in Me_2SO, ethyl 2-(ethoxycarbonyl)-4,4-dimethyl-3-oxopentanoate (**27**)[13] was obtained in 31% yield together with a minor product of **22b** (6% yield, Scheme IV).

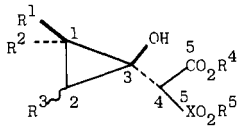
Treatment of **9a** with 1 equiv of Br_2 caused a skeletal rearrangement[14] in a Favorskii fashion in parallel with bromination to give ethyl 5-bromo-4,4-dimethyl-2-(ethoxycarbonyl)-3-oxopentanoate (**30**) in 76% yield (Scheme V). This compound has been synthesized in an alternative way from 3-bromo-2,2-dimethylpropanoyl chloride (**28**)[15] and ethyl ethoxymagnesium malonate (**29**). Compound **30** was cyclized to 2-[bis(ethoxycarbonyl)methylidene]-3,3-dimethyloxetane (**31**) in 77% yield by treatment with NaH in THF.

Several attempts to extend this reaction to other carbanions have not been successful[16] so far. The reaction of **6a** with ethyl cyanoacetate (NaH) gave ethyl 2-cyano-3,3-dimethyl-4-oxopentanoate (**32**). It is worthwhile to note here that the reaction of **6a** and ethyl (phenylthio)acetate (**33**)[17] in the presence of lithium diisopropylamide (LDA)

(9) Dressler, H.; Graham, J. E. *J. Org. Chem.* **1967**, *32*, 985.
(10) Laboratory work by Mr. Junichi Tanabe.

(11) By treatment with CH_2N_2, compound **24** was converted into the corresponding methyl ester: Gunter, R.; Immo, B.; Quirin, S. German Offen. 2412784, 1975; *Chem. Abstr.* **1975**, *84*, 43341.
(12) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S. *J. Org. Chem.* **1976**, *41*, 260.
(13) The IR and ^1H NMR spectra of **27** were identical with those of a sample which was alternatively prepared from pivaloyl chloride and ethyl ethoxymagnesium malonate.
(14) Depuy, C. H.; Arney, W. C., Jr.; Gibson, D. H. *J. Am. Chem. Soc.* **1968**, *90*, 1830.
(15) Nerdel, F.; Weyerstahl, P.; Kretzschmar, U. *Chem. Ber.*, **1959**, *92*, 1329.
(16) Both ethyl acetoacetate (NaH) and cyclopentadiene (NaH) gave a complex, uncharacterizable material. Ylides such as dimethyloxosulfonium (ethoxycarbonyl)methylide (Nozaki, H.; Tunemoto, D.; Matubara, S.; Kondo, K. *Tetrahedron* **1967**, *23*, 545) and dimethyloxosulfonium bis(ethoxycarbonyl)methylide (Ando, W.; Yagihara, T.; Tozune, S.; Imai, I.; Suzuki, J.; Toyama, T.; Nakaido, S.; Migita, T. *J. Org. Chem.* **1972**, *37*, 1721) were unreactive.
(17) Horn, C. F.; Vineyard, H. U.S. Patent 3116321 1963; *Chem. Abstr.* **1963**, *60*, P6792*d*.

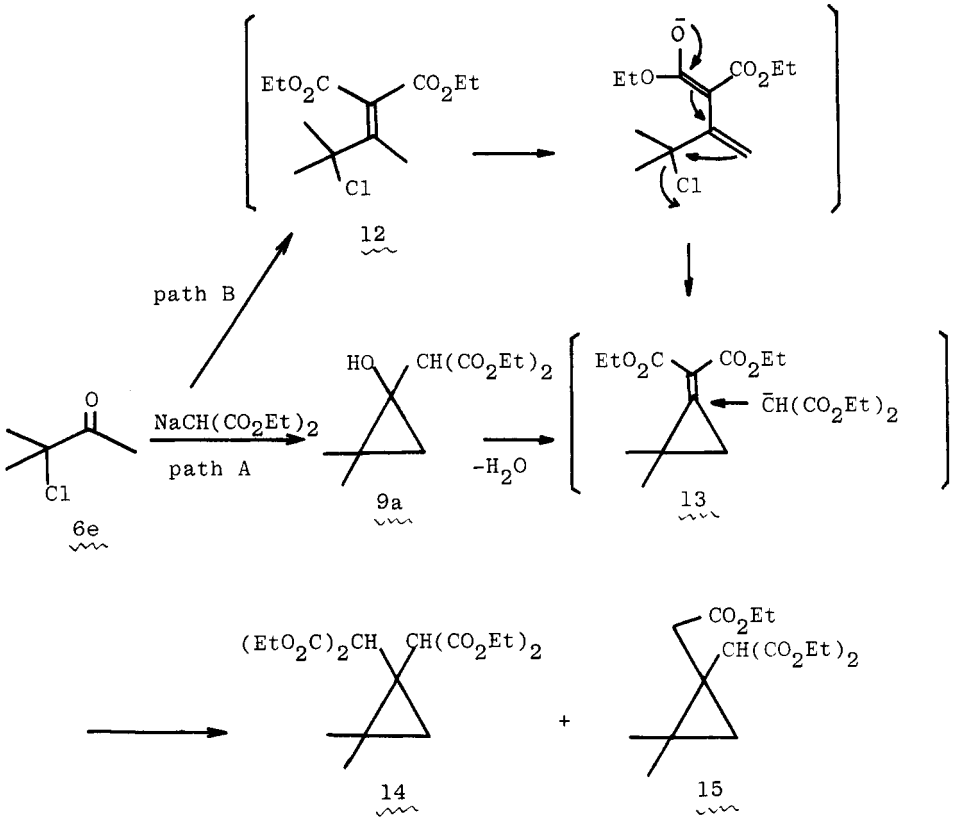
Table III. ^{13}C NMR Spectral Data ($CDCl_3$) of Cyclopropanols



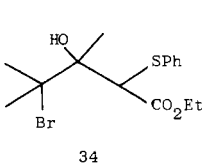
compd	chemical shift, ppm									
	C-1	C-2	C-3	C-4	C-5 (X)	R^1	R^2	R^3	R^4	R^5
9a	22.1	25.0	61.5	56.1	169.8	22.4	19.8		14.1, 61.7	14.1, 61.5
9b	22.5	26.4	61.6	56.9	169.7, 169.8	24.0	14.1	6.6	14.1, 61.6	14.2, 61.6
9c	29.5	23.5	62.3	55.5	169.3, 170.1	25.2, 25.5, 26.4 29.8, 32.7			14.1, 61.7	14.1, 61.7
9d	33.2	25.4	60.6	56.8	169.3, 169.7	26.5, 27.1, 31.2 33.2			14.1, 61.7	14.1, 61.7
16	21.8 (24.1)	25.8	59.2 (60.0)	73.9 (73.7)	166.2	22.1 (23.0)	19.4 (19.6)[a]		14.0, 62.6	[b]
18	22.4	24.9	61.7 (61.6)	55.9 (55.8)	169.8 (169.5),[a] 172.7 (172.8)	22.2	19.8		14.0, 62.0	
23[c]	22.5	25.2	62.0	55.9	171.5, 171.0	22.3	20.2			

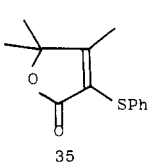
[a] Paired signals in the parentheses (60% of relative intensity) indicate the presence of two diastereomers. [b] Signals due to phenyl carbons: 138.9 (139.1)[a] (s), 129.4 (129.2) (d), 128.8 (d), and 134.1 ppm (d). [c] CD_3COCD_3.

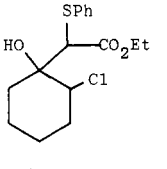
Scheme II



gave ethyl 4-bromo-3,4-dimethyl-3-hydroxy-2-(phenylthio)pentanoate (**34**, 14% yield) and 4,5,5-trimethyl-3-







(phenylthio)-2(5*H*)-furanone (**35**, 12% yield). Furthermore, similar reaction of **33** with 1 afforded ethyl 2-chloro-1-hydroxy-α-(phenylthio)cyclohexaneacetate (**36**) in 81% yield.

Experimental Section

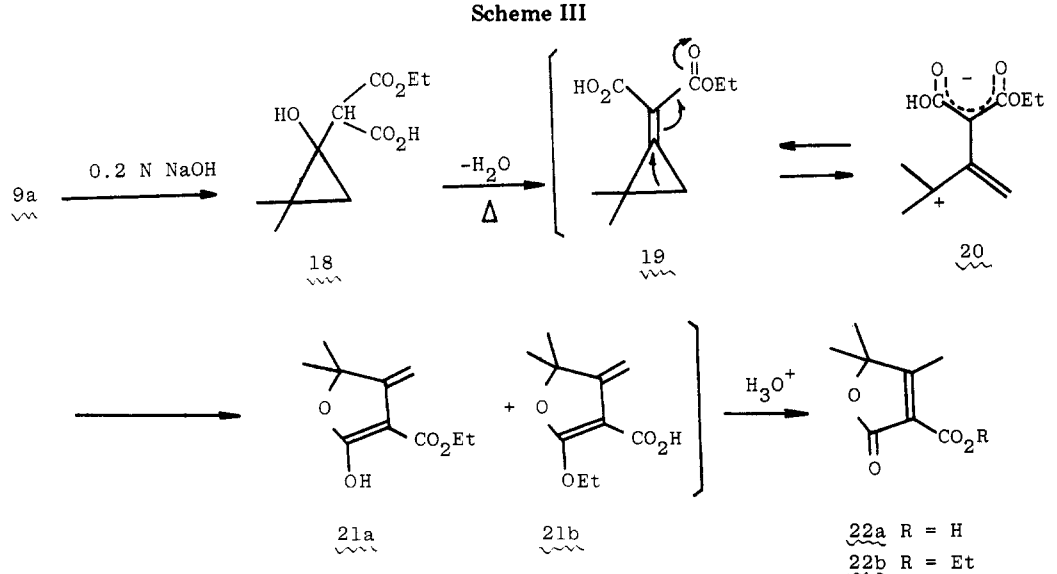
Melting points were determined on a Yamato Model MP-21 melting point apparatus and are uncorrected. The evaporative bulb-to-bulb distillations were done by using a Büchi Kugelrohrofen apparatus at the pressure and oven temperature indicated. Elemental analysis was carried out by Mr. Eiichiro Amano of our laboratory. IR spectra were determined on a Hitachi Model EPI-S2 spectrometer. Mass spectra were recorded at 70 eV with a Hitachi Model RMS-4 mass spectrometer and ^1H NMR spectra at 60 MHz with a Hitachi Model R-24 spectrometer. Both ^1H

Table IV. Boiling Points and Spectral Data of γ-Keto Esters 10f-n

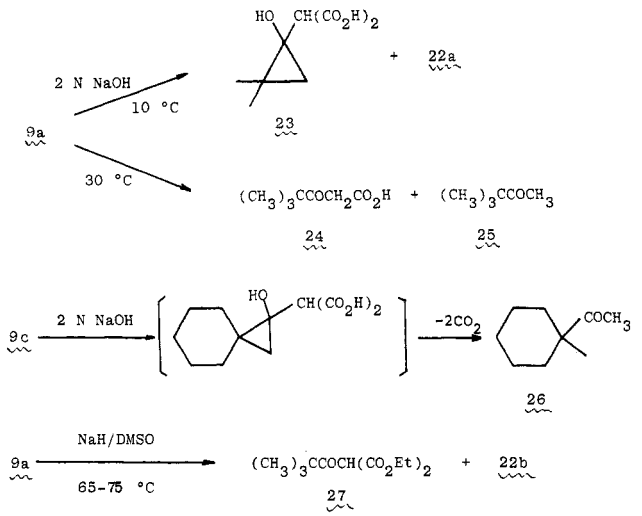
compd	bp, °C	IR, cm^{-1}	^1H NMR (CCl_4), δ	^{13}C NMR ($CDCl_3$), ppm
10f[a,j]	153-155 (3)	1730	1.11 (d, 6 H, J = 7 Hz, 2 CH_3), 1.28 (t, 6 H, J = 7 Hz, ester 2 CH_3), 2.62 (m, 1 H, C_5 H), 2.91 (d, 2 H, J = 8 Hz, C_3 H), 3.73 (t, 1 H, J = 8 Hz, C_2 H), 4.16 (q, 4 H, J = 7 Hz, ester 2 CH_2)	13.8 (q, ester CH_3), 17.9 (q, C_6 and 5-CH_3), 38.8 (t, C_3), 40.5 (d, C_5), 46.8 (d, C_2), 61.4 (t, ester CH_2), 169.0 (s, ester C=O), 211.0 (s, C=O)
10g[b]	107-111 (3)	1745, 1725	1.27 (t, 6 H, J = 7 Hz, ester 2 CH_3), 2.16 (s, 3 H, CH_3), 2.91 (d, 2 H, J = 7 Hz, C_3 H), 3.72 (t, 1 H, J = 7.5 Hz, C_2 H), 4.17 (q, 4 H, J = 7 Hz, ester 2 CH_2)	14.1 (q, ester CH_3), 29.6 (q, C_5), 42.1 (t, C_3), 47.2 (d, C_2), 61.7 (t, ester CH_2), 169.1 (s, ester C=O), 205.1 (s, C=O)
10i[c]	114-131 (3)	1740, 1720	1.08 (t, 3 H, J = 7 Hz, CH_3), 1.29 (t, 6 H, J = 7 Hz, ester 2 CH_3), 2.46 (q, 2 H, J = 7 Hz, C_5 H), 2.89 (d, 2 H, J = 7 Hz, C_3 H), 3.78 (t, 1 H, J = 7 Hz, C_2 H), 4.19 (q, 4 H, J = 7 Hz, ester 2 CH_2)	
10j[d]	110-120 (3)	1740, 1720	[h]1.14 (d, 3 H, J = 7 Hz, CH_3), 1.24 (t, 3 H, J = 7 Hz, ester CH_3), 1.28 (t, 3 H, J = 7 Hz, ester CH_3), 2.26 (s, 3 H, $COCH_3$), 3.30 (m, 1 H, C_3 H), 3.74 (d, 1 H, J = 10 Hz, C_2 H), 4.15 (q, 2 H, J = 7 Hz, ester CH_2), 4.22 (q, 2 H, J = 7 Hz, ester CH_2)	14.0 (q, ester CH_3), 14.1 (q, ester CH_3), 14.4 (q, 3-CH_3), 28.6 (q, C_5), 45.6 (d, C_2), 54.6 (d, C_3), 61.6 (t, ester CH_2), 168.7 (s, ester C=O), 209.6 (C=O)
10l[e,j]	120-136 (3)	1735, 1715	0.88 (d, 3 H, J = 7 Hz, CH_3), 0.94 (d, 3 H J = 7 Hz, CH_3), 1.25 (t, 3 H, J = 7 Hz, ester CH_3), 1.28 (t, 3 H, J = 7 Hz, ester CH_3), 1.80 (m, 1 H, CH), 2.22 (s, 3 H, CH_3), 3.18 (dd, 1 H, CH), 3.75 (d, 1 H, J = 11 Hz, C_2 H), 4.10 (q, 2 H, J = 7 Hz, ester CH_2), 4.15 (q, 2 H, J = 7 Hz, ester CH_2)	14.0 (q, ester CH_3), 14.1 (q, ester CH_3), 18.0 (q, CH_3), 21.1 (q, CH_3), 28.4 (d, CH), 32.5 (q, C_5), 53.1 (d, C_2), 55.7 (d, C_3), 61.5 (t, CH_2), 61.6 (t, CH_2), 168.7 (s, C=O), 168.9 (s, C=O), 209.2 (s, C=O)
10m[f,j]	[i]	1735, 1710	1.26 (t, 9 H, J = 7 Hz, ester 3 CH_3), 1.30 (s, 6 H, 2 CH_3), 3.55 (s, 1 H), 3.87 (s, 2 H), 4.16 (q, 6 H, ester 3 CH_2)	14.6 (q, ester 3 CH_3), 22.5 (q, 2 CH_3), 45.1 (t, C_2), 48.9 (s, C_4), 58.4 (d), 61.4 (t, ester CH_2), 61.5 (t, ester CH_2), 168.1 (s, ester C=O), 206.5 (s, C=O)
10n[g,j]	[i]	1735	1.28 (t, 9 H, J = 7 Hz, ester 3 CH_3), 1.62 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 4.26 (q, 6 H, J = 7 Hz, ester 3 CH_2), 4.32 (s, 1 H CH)	

[a] Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.62; H, 8.16. [b] Kishimoto, H.; Kuroda, T.; Sakaki, I.; Kamimori, S. *Japan Kokai* **1975**, *59*, 322; *Chem. Abstr.* **1975**, *83*, p78621. [c] Temnikova, T. I.; Semenova, S. N. *Zh. Obshch. Khim.* **1965**, *35*, 27. [d] Kiyooka, S.; Hase, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3609. [e] Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.38; H, 8.90. [f] Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 56.70; H, 7.46. [g] Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.34; H, 7.34. [h] $CDCl_3$. [i] Isolated by TLC on silica gel (hexane-acetone, 3:1). [j] Compound is new.

Scheme III



Scheme IV



NMR (100 MHz) spectra and ^{13}C NMR (25 MHz) spectra were taken in $CDCl_3$ on a JEOL Model FX-100 spectrometer equipped with FT facilities and using Me_4Si as an internal standard. The off-resonance decoupling was used to support the assignment. The analytical determination and the preparative isolation by GLC were performed on a Hitachi Model K-53 gas chromatograph and a Yanagimoto Model GCG-550T gas chromatograph, respectively. Preparative isolations by high-performance liquid chromatography (HPLC) were done with a Yanagimoto Model L-2000 high-performance liquid chromatograph using a column of Yanapac SA-II (4ϕ × 250 mm). TLCs were done on silica gel (Kieselgel 60 PF_{254}, Merck A. G., Darmstadt) with layers of 0.25- and 1.00-mm thickness, respectively. Column chromatography was performed on a column containing silica gel (Wakogel C-200, Wako Junyaku Kogyo Co. Ltd.).

Halo ketones 1,[18] **6a**,[19] **6b**,[19] **6c**,[20] **6d**,[21] **6e**,[19] **6f**,[19] **6i**,[22] **6k**,[22] **6l**,[19] **6m**,[23] **6n**,[24] **6o**,[25] and **6p**[26] were prepared by procedures described in the literature. Halo ketones such as **6g**, **6h**, and **6j** were obtained from commercial sources.

The following experiments with **9a** illustrate the manner in which reactions of **6** and enolate anions were carried out.

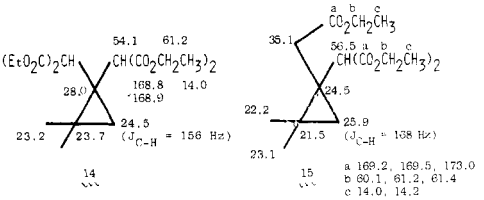
1-[Bis(ethoxycarbonyl)methyl]-2,2-dimethylcyclopropanol (9a). Procedure A. Sodium hydride (0.954 g, 39.4 mmol) was added to a solution of ethyl malonate (6.30 g, 39.4 mmol) in dry THF (30 mL). The mixture was heated under reflux for 4 h. A solution of **6a** (6.50 g, 39.4 mmol) in dry THF (15 mL) was added dropwise to the cold mixture at 0 °C. After being stirred for 17 h under reflux, the resulting mixture was poured into water and acidified with 10% HCl. The organic layer was extracted with ether and dried over $MgSO_4$. Evaporation of the solvent left 7.82 g of an oil, which was subjected to vacuum distillation [bp 97–110 °C (1 mm)] to give 4.92 g (51% yield) of **9a** (see Tables II and III for spectral data). The analytical sample of **9a** was obtained by column chromatography on silica gel (benzene–2-propanol, 30:1) followed by bulb-to-bulb distillation. The same reaction with 2 equiv of **2** in THF afforded **9a** in 61% yield.

Procedure B. The similar reaction of **6a** with 1 equiv of **2** in refluxing benzene for 12 h gave **9a** in 64% yield together with a small amount (2% yield) of 2(5*H*)-furanone **22b**: IR (neat)[7] 1765, 1710, 1645 cm^{-1}; ^1H NMR (CCl_4)[7] δ 1.37 (t, 3 H, J = 7 Hz, ester CH_3), 1.48 (s, 6 H, 2 5-CH_3), 2.30 (s, 3 H, 4-CH_3), 4.29 (q, 2 H, J = 7 Hz, ester CH_2); ^{13}C NMR ($CDCl_3$) 13.0 (q, 4-CH_3), 14.1 (q, ester CH_3), 24.3 (q, 2 5-CH_3), 61.1 (t, ester CH_2), 85.3 (s, C-5), 118.1 (s, C-3), 161.5 (s, C-4), 167.2 (s, ester C=O), 180.2 ppm (s, C-2).

1-[(Benzenesulfonyl)(ethoxycarbonyl)methyl]-2,2-dimethylcyclopropanol (16). A suspension of ethyl benzenesulfonyl acetate (2.06 g, 9 mmol) and NaH (217 mg, 9 mmol) in 20 mL of THF was heated under reflux for 2.5 h. A solution of **6a** (1.31 g, 7.9 mmol) in THF (2 mL) was added dropwise to the cold mixture at 0 °C. After being stirred for 1 h at 0 °C and for an additional 17 h under reflux, the resulting mixture was worked up as usual to give 2.64 g of an oil. It was separated by column chromatography on silica gel (benzene–methanol, 30:1) to afford 962 mg (39% yield) of **16** (See Tables II and III for spectral data) together with 187 mg (9% yield) of 3-(benzenesulfonyl)-4,5,5-trimethyl-2(5*H*)-furanone (**17**): mp 158.9–159.5 °C (ether); IR (KBr) 1750, 1625, 1325, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 6 H, 2 CH_3), 2.49 (s, 3 H, 4-CH_3), 7.4–8.2 (m, 5 H, C_6H_5); ^{13}C NMR ($CDCl_3$) 12.5 (q, 4-CH_3), 24.1 (q, 5-CH_3), 86.6 (s, C-5), 126.5 (s, C-3), 128.4 (d), 129.1 (d), 134.3 (d), 139.2 (s), 164.5 (s, C-4), 179.3 ppm (s, C-2). Anal. Calcd for $C_{13}H_{14}O_4S$: C, 58.63; H, 5.30. Found: C, 58.73; H, 5.53.

Reaction of 6e with 2. To a stirred suspension of ethyl malonate (830 mg, 5.19 mmol) and NaH (124 mg, 5.19 mmol) in 10 mL of THF was added with caution 350 mg (2.90 mmol) of **6e** at 0 °C. After being stirred for 17 h under reflux, the mixture was acidified with 10% HCl. The organic layer was extracted with ether and dried over $MgSO_4$. Evaporation of the solvent left 877 mg of an oil, which was fractionated to four components by preparative HPLC (hexane–ether, 10:1; 1.70 mL/min). The fraction, retention time, integrated percentage, and composition were as follows: fraction 1, 6.2 min, 15%, ethyl malonate; fraction 2, 8.7 min, 35%, 1-[bis(ethoxycarbonyl)methyl]-2,2-dimethyl-1-[(ethoxycarbonyl)methyl]cyclopropane (**15**); fraction 3, 11 min, 9%, **9a**; fraction 4, 16 min, 37%, 1,1-bis[bis(ethoxycarbonyl)-methyl]-2,2-dimethylcyclopropane (**14**). For cyclopropane **14**: yield 29% (HPLC); IR (neat) 1750, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.71 (s, 2 H, 2 C-3 H), 1.25 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.27 (s, 6 H, 2 CH_3), 1.28 (t, 6 H, J = 7 Hz, ester 2 CH_3), 3.90 (s, 2 H, 2 α-CH of ester), 4.16 (q, 4 H, J = 7 Hz, ester 2 CH_2), 4.17 (q, 4 H, J = 7 Hz, ester 2 CH_2). Anal. Calcd for $C_{19}H_{30}O_8$: C, 59.05; H, 7.82. Found: C, 59.20; H, 7.90. For cyclopropane **15**: yield 34% (HPLC); IR (neat) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.59 (s, 2 H, 2 C-3 H), 1.14 (s, 3 H, 2-CH_3), 1.17 (s, 3 H, 2-CH_3), 1.22 (t, 3 H, J = 7 Hz, ester CH_3), 1.26 (t, 3 H, J = 7 Hz, ester CH_3), 1.27 (t, 3 H, J = 7 Hz, ester CH_3), 2.81 (s, 2 H, CH_2CO_2Et), 3.12 (s, 1 H, α-CH of ester), 4.06 (q, 2 H, J = 7 Hz, ester CH_2), 4.18 (q, 2 H, J = 7 Hz, ester CH_2), 4.35 (q, 2 H, J = 7 Hz, ester CH_2); mass spectrum, m/e (relative intensity) 269 (M – OEt, 7), 241 (M – CO_2Et, 15). Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found: C, 61.03; H, 8.13.

The ^{13}C NMR spectral data ($CDCl_3$, ppm) of compounds **14** and **15** are summarized in the following structures.



The similar reaction of **6e** with 1 equiv of **2** yielded **9a** (21% yield), **15** (7% yield), and a trace of **14**. The similar reaction of **6e** using 2.2 equiv of **2** in refluxing benzene for 65 h afforded only a trace of **9a** in addition to **14** (9% yield) and **15** (22% yield).

Reaction of 9a with 2. Cyclopropanol **9a** (285 mg, 1.17 mmol) was allowed to react with 1 equiv of **2** (190 mg of ethyl malonate and 28 mg of NaH) in 10 mL of THF under reflux for 16 h. After the mixture was poured into water and acidified with 10% HCl, it was extracted with ether. Workup in a usual manner gave 337 mg of yellow oil, whose composition was shown by HPLC (hexane–ether, 10:1) to be ethyl malonate (59% recovered), **15** (12% yield), **9a** (42% recovered), and **14** (15% yield).

Ethyl 4-Chloro-3,4-dimethyl-2-(ethoxycarbonyl)-2-pentenoate (12). To a stirred solution of $TiCl_4$ (10 mL, 90 mmol) in

(18) Newman M. S.; Farbman, M. D.; Hipsher, H. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 188.
(19) Thorpe, J. W.; Warkentin, J. *Can. J. Chem.* **1973**, *51*, 927.
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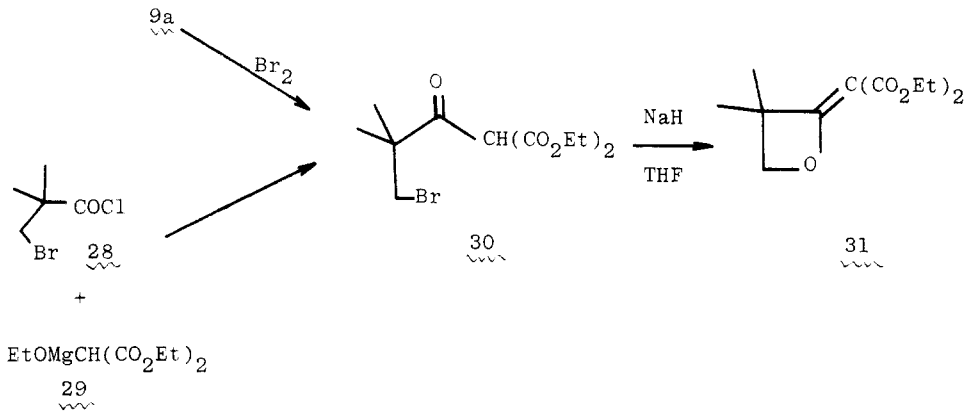
(24) Aufauvre, Y.; Verney, M.; Vessiere, R. *Bull. Soc. Chem. Fr.* **1973**, 1373.
(25) Sacks, A. A.; Aston, J. G. *J. Am. Chem. Soc.* **1951**, *73*, 3902.
(26) Fitjer, L. *Synthesis* **1977**, 189.

Scheme V



100 mL of 5:1 THF–CCl_4 was added a mixture of ethyl malonate (8.0 g, 50 mmol) and the chloro ketone **6e** (6.0 g, 50 mmol). Pyridine (15.8 g) was added to the mixture dropwise within 35 min. After being stirred for 20 h at room temperature, the mixture was treated in the usual manner.[8] Vacuum distillation gave 2.06 g (20%) of product: bp 90–115 °C (3 mm); IR (neat) 1725, 1625 cm^{-1}; ^1H NMR (CCl_4) δ 1.29 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.81 (s, 6 H, 2 CH_3), 2.14 (s, 3 H, $(C{=}CH_2)CH_3$), 4.14 (q, 4 H, J = 7 Hz, ester 2 CH_2). Anal. Calcd for $C_{12}H_{19}O_4Cl$: C, 54.86; H, 7.29. Found: C, 54.64; H, 7.36.

Reaction of 12 with 2. A mixture of the ester **12** (134 mg, 0.51 mmol) and a solution of **2** (1.0 mmol) in THF [ethyl malonate (160 mg), NaH (24 mg), THF (6 mL)] was refluxed for 57 h. The resulting mixture was poured into water and acidified with 10% HCl. Workup in a usual manner gave 215 mg of crude product. Preparative TLC on silica gel (hexane–acetone, 6:1) gave 6 mg of **14** (R_f 0.41–0.66, 3% yield) and 13 mg of the furanone **22b** (R_f 0.23, 13% yield).

Hydrolysis of 9a with 0.2 N NaOH. Acid Ester 18. A suspension of **9a** (1.0 g, 4.1 mmol) in 30 mL of 0.2 N NaOH was stirred for 24 h at room temperature. After the unreacted **9a** (15 mg) was removed by extraction with ether, the aqueous layer was acidified with 10% HCl. The resulting organic layer was extracted with ether and dried over $MgSO_4$. Removal of the solvent left 622 mg (70% yield) of acid ester **18**: IR (neat) 3400, 3400–2500, 1730 cm^{-1}; ^1H NMR (CCl_4) δ 0.54 (d, 1 H, J = 6 Hz, C-3 H), 0.69 (d, 1 H, J = 6 Hz, C-3 H), 1.06 (s, 3 H, 2-CH_3), 1.20 (s, 3 H, 2-CH_3), 1.29 (t, 3 H, J = 7 Hz, ester CH_3), 3.22 (s, 1 H, α-CH of ester), 4.25 (q, 2 H, J = 7 Hz, ester CH_2), 7.30 (br s, 2 H, OH and CO_2H). It was not stable to get acceptable elemental analysis.

Pyrolysis of the Acid Ester 18. Furanones 22a and 22b. Compound **18** (315 mg, 1.5 mmol) was heated at 200 °C for 30 min on an oil bath. After cooling to room temperature, the reaction mixture was neutralized with aqueous $NaHCO_3$. The neutral portion was extracted with ether to give 113 mg (39%) of furanone **22b**. After being acidified with 10% HCl, the aqueous layer was treated with ether. Evaporation of the solvent gave 67 mg (27%) of furanone **22a**: mp 107–107.8 °C (lit.[7] mp 112–113 °C); IR (KBr) 3500–2500, 1753, 1700, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, 6 H, 2 CH_3), 2.51 (s, 3 H, 4-CH_3), 8.8 (br s, 1 H, OH); ^{13}C NMR ($CDCl_3$) 13.3 (q, 4-CH_3), 24.0 (q, 2 5-CH_3), 89.1 (s, C-5), 114.7 (s, C-3), 155.2 (s, C-4), 160.2 (s), 172.4 (s).

Pyrolysis of 9a. Cyclopropanol **9a** (338 mg, 1.6 mmol) was heated at 200 °C in an oil bath until the evolution of CO_2 ceased. The resulting oil was separated by column chromatography on silica gel (hexane–acetone, 10:1) to give 145 mg (46%) of the furanone **22b**.

Hydrolysis of 9a with 2 N NaOH at 10 °C. 1-(Dicarboxymethyl)-2,2-dimethylcyclopropanol (23). Cyclopropanol **9a** (1.0 g, 4.1 mmol) was stirred with 80 mL of 2 N NaOH for 24 h at 10 °C. After being acidified with 10% HCl, the organic layer was extracted with ether and dried over $MgSO_4$. Removal of the solvent left 463 mg (60%) of crude product **23**: mp 96.9–98.0 °C dec ($CHCl_3$); IR (KBr) 3600–2300, 3400, 1730 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 0.57 (d, 1 H, J = 6 Hz, C-3 H), 0.65 (d, 1 H, J = 6 Hz, C-3 H), 1.15 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 3.39 (s, 1 H, α-CH of ester), 4.0–7.0 (br s, 3 H, OH and 2 CO_2H); mass spectrum, m/e (relative intensity) 137 (8), 126 (M – CO_2 – H_2O, 7), 111 (21), 100 (M – 2 CO_2, 11), 83 (14), 67 (17), 57 (54), 43 (100). Anal. Calcd for $C_8H_{12}O_5$: C, 51.06; H, 6.43. Found: C, 51.13; H, 6.48. After the aqueous layer was evaporated to dryness, the residue was extracted with ether to give 184 mg (27%) of the furanone **22a**.

Hydrolysis of 9a with 2 N NaOH at 30 °C. Cyclopropanol **9a** (1.0 g, 4.1 mmol) was stirred with 80 mL of 2 N NaOH for 26 h at 30 °C. The organic layer was extracted with ether and dried over $MgSO_4$. Careful evaporation of the solvent at atmospheric pressure left 74 mg (18%) of 3,3-dimethyl-2-butanone. After the aqueous layer was acidified with 10% HCl, the organic layer was extracted with ether and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure gave 224 mg (38%) of β-keto acid **24**: IR (neat) 3500–2300, 1700 cm^{-1}; ^1H NMR (CCl_4) δ 1.17 (s, 9 H, 3 CH_3), 3.49 (s, 1 H, C-2 H), 4.98 (s, 0.5 H, enol C-2 H), 10.19 (br s, 1 H, OH), 12.09 (br s, 0.5 H, enol OH). Anal. Calcd for $C_7H_{12}O_3$: C, 58.32; H, 8.39. Found: C, 58.11; H, 8.25.

1-Acetyl-1-methylcyclohexanone (26). A suspension of **9c** (335 mg, 1.18 mmol) in 23 mL of 2 N NaOH was stirred for 24 h at room temperature. After being acidified with 10% HCl, the organic layer was extracted with ether and dried over $MgSO_4$. Removal of the solvent gave 153 mg of viscous oil, which was subjected to vacuum distillation [bp 83–115 °C (48 mm)] to give 84 mg (51%) of **26**. The IR and ^1H NMR spectra of this product were identical with those reported.[12]

Treatment of 9a with NaH in Me_2SO. Cyclopropanol **9a** (301 mg, 1.23 mmol) was added to the stirred suspension of NaH (34 mg, 1.44 mmol) in 5 mL of Me_2SO at room temperature. After being stirred for 12 h at 65–75 °C, the resulting mixture was poured into water, acidified with 10% HCl, and extracted with ether. After the removal of the solvent, the residue was fractionated by preparative TLC on silica gel (benzene–AcOEt, 10:1) to afford 93 mg (31%, R_f 0.87) of ethyl 4,4-dimethyl-2-(ethoxycarbonyl)-3-oxopentanoate (**27**) together with 16 mg (6%, R_f 0.35) of furanone **22b**. For ester **27**: bp 120–133 °C (3 mm); IR (neat) 1750 cm^{-1}; ^1H NMR (CCl_4) δ 1.16 (s, 9 H, 3 CH_3), 1.29 (t, 6 H, J = 7 Hz, ester 2 CH_3), 4.21 (q, 4 H, J = 7 Hz, 2 CH_2), 4.69 (s, 1 H, C-2 H); ^{13}C NMR ($CDCl_3$) 13.5 (q, ester 2 CH_3), 25.4 (q, 3 CH_3), 45.1 (s, C-4), 59.3 (d, C-2), 61.7 (t, ester CH_2), 164.2 (s, ester C=O), 203.1 ppm (s, C=O). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 59.09; H, 7.96.

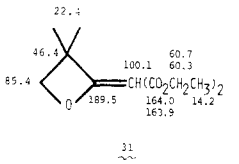
Alternative Preparation of 27. The mixture of magnesium turnings (0.6 g, 23 mmol), 0.5 mL of ethanol, and 0.05 mL of CCl_4 was heated under reflux. When the magnesium turnings began to dissolve, 15 mL of ether was added. To the mixture was added a solution of ethyl malonate (3.6 g, 22 mmol) in 4.5 mL of ethanol–ether (4:5) with caution. After the mixture refluxed for 3.5 h, the magnesium turnings were completely dissolved. To the resulting solution was then added a solution of pivaloyl chloride (2.9 g, 21 mmol) in 5 mL of ether within 15 min. After being stirred for 24 h under reflux, the reaction mixture was treated with 30 mL of 2 N H_2SO_4. The organic material was extracted with ether. Workup in a usual manner gave 4.51 g of yellow oil. It was subjected to vacuum distillation [bp 120–133 °C (3 mm)] to afford 4.14 g (77% yield) of **27**.

Ethyl 5-Bromo-4,4-dimethyl-2-(ethoxycarbonyl)-3-oxopentanoate (30). To a solution of **9a** (1.03 g, 4.2 mmol) in 3 mL of CCl_4 was added Br_2 (0.26 mL, 5.0 mmol) dropwise, and the

mixture was stirred for 6 h at room temperature. After removal of the solvent, the residual oil was diluted with water. The organic layer was extracted with ether and dried over $MgSO_4$. Evaporation of the solvent left 1.45 g of yellow oil. Purification of this product by column chromatography on silica gel (hexane–acetone, 30:1) followed by vacuum distillation [bp 110–114 °C (1 mm)] gave 1.04 g (76% yield) of the bromo ester **30**: IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.32 (s, 6 H, 2 4-CH_3), 3.49 (s, 2 H, 2 5-H), 4.23 (q, 4 H, J = 7 Hz, ester 2 CH_2), 4.87 (s, 1 H, α-CH of ester); mass spectrum, m/e (relative intensity) 242 (M – HBr, 0.6), 187 (M – C_4H_8Br, 12), 160 ($CH_2(CO_2Et)_2$, 4); ^{13}C NMR ($CDCl_3$) 13.9 (q, ester 2 CH_3), 23.3 (q, 2 CH_3), 40.2 (t, CBr), 51.2 (s, C-4), 61.0 (d, C-2), 62.5 (t, ester 2 CH_2), 164.4 (s, ester 2 C=O), 201.5 ppm (C=O). Anal. Calcd for $C_{12}H_{19}O_5Br$: C, 44.42; H, 5.83. Found: C, 44.60; H, 5.93.

2-[Bis(ethoxycarbonyl)methylidene]-3,3-dimethyloxetane (31). To a suspension of NaH (85 mg, 3.5 mmol) in 2 mL of THF was added a solution of the bromo ester **30** (1.10 g, 3.4 mmol) in 3 mL of THF. After being stirred for 4 h at room temperature, the solvent was removed under reduced pressure. The residual oil was acidified with 10% HCl, extracted with ether, and dried over $MgSO_4$. Removal of the solvent left 0.63 g of yellow oil. Purification of this product by column chromatography on silica gel (hexane–acetone, 10:1) followed by vacuum distillation [bp 115–118 °C (2 mm)] gave 631 mg (77% yield) of the oxetane **31**: IR (neat) 1710, 1640 cm^{-1}; ^1H NMR (CCl_4) δ 1.29 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.57 (s, 6 H, 2 3-CH_3), 4.14 (q, 4 H, J = 7 Hz, ester 2 CH_2), 4.58 (s, 2 H, ring 2 H). Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.23; H, 7.31.

The ^{13}C NMR spectrum ($CDCl_3$, ppm) is summarized in the following structure.



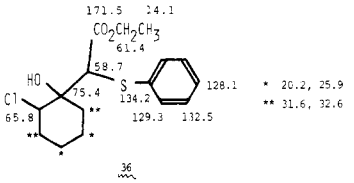
Alternative Preparation of the Bromo Ester 30. Ethyl ethoxymagnesium malonate, which was prepared from ethyl malonate (0.88 g, 5.5 mmol), magnesium turnings (0.15 g, 5.7 mmol), and ethanol (0.8 mL), was allowed to react with the acid chloride **28**[15] (0.98 g, 4.9 mmol) in a manner similar to that for the preparation of **27**, giving 431 mg (27% yield) of the bromo ester **30**.

Ethyl 2-Cyano-3,3-dimethyl-4-oxopentanoate (32). To a stirred suspension of ethyl cyanoacetate (93 mg, 0.83 mmol), NaH (20 mg, 0.83 mmol), and 15-crown-5[27] (48 mg, 0.22 mmol) in 10 mL of THF was added a solution of **6a** (125 mg, 0.76 mmol) in 2 mL of THF at room temperature. After being stirred for 19 h at room temperature, the mixture was acidified with 10% HCl. The organic layer was extracted with ether and dried over $MgSO_4$. Evaporation of the solvent left 124 mg of an oil. Preparative TLC on silica gel (hexane–acetone, 10:1) gave 27 mg (18%) of product **32**: IR (neat) 2250, 1745, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (t, 3 H, J = 7 Hz, ester CH_3), 1.34 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 2.26 (s, 3 H, $COCH_3$), 4.16 (s, 1 H, C-2 H), 4.24 (q, 2 H, J = 7 Hz, ester CH_2). Anal. Calcd for $C_{10}H_{15}O_3N$: C, 60.90; H, 7.67. Found: C, 60.76; H, 7.71.

Reaction of 6a with Ethyl (Phenylthio)acetate (33). Ethyl 4-Bromo-3,4-dimethyl-3-hydroxy-2-(phenylthio)pentanoate (34) and 4,5,5-Trimethyl-3-(phenylthio)-2(5*H*)-furanone (35). To a stirred solution of 3.7 mmol of LDA [prepared from 3.7 mmol of butyllithium (1.5 M hexane solution) and diisopropylamine (380 mg, 3.7 mmol)] in 3 mL of THF was added dropwise the ester **33** (740 mg, 3.7 mmol) at –65 °C. After the mixture was stirred for 1 h at –65 °C, a solution of the bromide **6a** (620 mg, 3.7 mmol) in 6 mL of THF was added with caution. The stirring was continued for an additional 1.5 h at –65 °C. The resulting mixture was then poured into water and treated with aqueous NH_4Cl. The organic layer was extracted with ether and dried over $MgSO_4$. Evaporation of the solvent left 980 mg of an oil, which was separated by preparative TLC on silica gel (hexane–acetone, 10:1) to give 187 mg (14%) of the bromohydrin **34** (R_f 0.45) together with 85 mg (12%) of the 2(5*H*)-furanone **35** (R_f 0.20). For bromohydrin **34**: IR (neat) 3500, 1730, 1580, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (s, 3 H, CH_3), 1.23 (t, 3 H, J = 7 Hz, ester CH_3), 1.26 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.57 (s, 1 H, C-2 H), 4.10 (br s, 1 H, OH), 4.14 (q, 2 H, J = 7 Hz, ester CH_2), 7.3 (m, 5 H, C_6H_5); ^{13}C NMR ($CDCl_3$) 14.2 (q, ester CH_3), 15.5 (q, 3-CH_3), 20.7 (q, CH_3), 21.1 (q, CH_3), 55.9 (d, C-2), 61.8 (t, ester CH_2), 63.3 (s, C-4), 64.1 (s, C-3), 128.5 (d), 129.4 (d), 133.5 (d), 133.5 (s), 170.1 ppm (s, C=O). It was not stable to get an acceptable elemental analysis. For 2(5*H*)-furanone **35**: IR (neat) 1760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (s, 6 H, 2 CH_3), 2.11 (s, 3 H, CH_3), 7.26 (m, 5 H, C_6H_5); ^{13}C NMR ($CDCl_3$) 12.8 (q, 4-CH_3), 24.9 (q, 2 5-CH_3), 86.6 (s, C-5), 120.6 (s, C-3), 127.1 (d), 129.4 (d, intensity four carbons), 133.5 (s), 170.0 (s, C-4), 175.2 ppm (s, C-2). Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 66.45; H, 6.21.

Ethyl 2-Chloro-1-hydroxy-α-(phenylthio)cyclohexaneacetate (36). Reaction of 2-chlorocyclohexanone (340 mg, 2.5 mmol) with the ester **33** (500 mg, 2.5 mmol) in the presence of 2.5 mmol of LDA dissolved in 5 mL of THF, which was carried out in the manner described in the foregoing experiment, gave 682 mg (83%) of **36**: bp 145–147 °C (0.08 mm); IR (neat) 3500, 1725, 1580, 1480 cm^{-1}; ^1H NMR (CCl_4) δ 1.17 (t, 3 H, J = 7 Hz, ester CH_3), 1.4–2.7 (m, 8 H, ring 4CH_2), 4.10 (q, 2 H, J = 7 Hz, ester CH_2), 4.14 (s, 1 H, α-CH of ester), 4.54 (t, 1 H, CHCl), 7.28 (m, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{21}O_3ClS$: C, 58.44; H, 6.44. Found: C, 58.39; H, 6.51.

The ^{13}C NMR spectrum ($CDCl_3$, ppm) is summarized in the following structure.



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Registry No. **1**, 822-87-7; **2**, 996-82-7; **6a**, 2648-71-7; **6b**, 18943-23-2; **6c**, 56077-27-1; **6d**, 3341-71-7; **6e**, 5950-19-6; **6f**, 19967-55-6; **6g**, 78-95-5; **6h**, 598-31-2; **6i**, 816-40-0; **6j**, 4091-39-8; **6k**, 814-75-5; **6l**, 29585-01-1; **6m**, 51287-60-6; **6n**, 37935-39-0; **9a**, 77320-47-9; **9b**, 77320-48-0; **9c**, 77320-49-1; **9d**, 77320-50-4; **10f**, 61337-00-6; **10g**, 23193-18-2; **10i**, 1907-97-7; **10j**, 77320-51-5; **10l**, 75002-91-4; **10m**, 77320-52-6; **10n**, 77320-53-7; **12**, 77320-54-8; **14**, 77320-55-9; **15**, 77320-56-0; **16** (isomer 1), 77320-57-1; **16** (isomer 2), 77320-58-2; **17**, 77320-59-3; **18**, 77320-60-6; **22a**, 13156-11-1; **22b**, 13156-09-7; **23**, 77320-61-7; **24**, 72531-41-0; **25**, 75-97-8; **26**, 2890-62-2; **27**, 22524-02-3; **28**, 2941-17-5; **29**, 35227-78-2; **30**, 77320-62-8; **31**, 77320-63-9; **32**, 23228-71-9; **33**, 7605-25-6; **34**, 77320-64-0; **35**, 77320-65-1; **36**, 77320-66-2; ethyl benzenesulfonylacetate, 7605-30-3; pivaloyl chloride, 3282-30-2; ethyl cyanoacetate, 105-56-6.

(27) In the absence of the catalyst, the reaction solely resulted in recovery of the starting materials.