Under the same conditions, the experimental results[12] found in the catalytic hydrogenation of acetophenone—kinetic order of 1 in hydrogen and of −0.5 in substrate—led us to think that the similar kinetic behavior for these two very dissimilar molecules may be due to the presence of the second hydrogenable function (benzenoid ring or carbonyl).

On the other hand, the initial selectivity in 4-hydroxycyclohexanone is only slightly affected by variations in the amount of substrate, the hydrogen pressure, or the amount of catalyst. In contrast, the temperature does affect the selectivity from 93% at 20 °C to 81% at 80 °C. A similar effect was also noted with respect to the nature of the solvent: 93% in 2-propanol, 86% in methanol, and 80% in water.

Generally, for a given metal, most of the factors which favor activity decrease the selectivity.

By utilizing ruthenium as the metal and 2-propanol as the solvent, we were able to obtain 4-hydroxycyclohexanone by hydrogenation *in a single step starting from the diketone with a yield of about 70%*.

In contrast, the majority of the prior preparations of this compound in homogeneous solution, whether from the diol[9,10,13] or the diketone,[14] take several steps and/or suffer from difficulties in extraction or separation, leading to decreasing yields.

Under these experimental heterogenous conditions it is possible to stop the hydrogenation at any time, and in particular, when the maximum yield of ketol has been reached.

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Registry No. 1,4-Cyclohexanedione, 637-88-7; 1,4-cyclohexanediol, 556-48-9; 4-hydroxycyclohexanone, 13482-22-9; Ni, 7440-02-0; Cu, 7440-50-8; Pd, 7440-05-3; Pt, 7440-06-4; Ir, 7439-88-5; Ru, 7440-18-8.

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Malonate Anion Induced Favorskii-Type Rearrangement. Reaction of Cyclic α-Halo Ketones with Sodiomalonates[1]

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The reaction of 2-chlorocyclohexanone (**1b**) with ethyl sodiomalonate in benzene at 0–25 °C gave 6-[bis(ethoxycarbonyl)methyl]bicyclo[3.1.0]hexan-6-ol (**4c**), the Favorskii-type intermediate, in 49% yield, in place of the substitution product ethyl *C*-(2-oxocyclohexyl)malonate (**3**). Derivatives of bicyclo[4.1.0]heptan-7-ol (**4a,b**) and those of bicyclo[3.1.0]hexan-6-ol (**4d,e**) were also obtained in good yields by similar means. Compound **4c** was transformed into **3** readily by heating with 0.05 equiv of NaH in benzene. The hydrolysis of **4a–d** with 0.2 N NaOH followed by pyrolysis at 110–120 °C gave the ring-contracted β-keto esters **9a–d**. Pyrolysis after the hydrolysis with 2 N NaOH gave the corresponding ketones **11a–d** in good yields. Oxidation of **4c** with CrO_3 and $HClO_4$ afforded ethyl *C*-(2-hydroxycyclopentanecarbonyl)malonate (**14**) in 45% yield. Treatment of **4c** with Br_2 gave ethyl *C*-(1-bromocyclopentanecarbonyl)malonate (**18**) in 64% yield.

The reaction of an α-halo ketone with hydroxide or alkoxide is well-known to give a carboxylic acid or ester via the Favorskii rearrangement.[2] On the other hand, the reaction of α-halo ketone with carbanions, such as sodiomalonate[3,4] and sodioacetoacetate,[5] has been reported to produce exclusively an α-substituted ketone via an S_N2 reaction.

Cocker[3] and Schemiakin[4] obtained ethyl *C*-(2-oxocyclohexyl)malonate (**3**) in the reaction of 2-chlorocyclohexanone (**1b**) with ethyl sodiomalonate (**2**) in benzene under reflux conditions. We carried the same reaction out at lower temperatures (0–25 °C) and contrarily obtained 6-[bis(ethoxycarbonyl)methyl]bicyclo[3.1.0]hexan-6-ol (**4c**) in 49% yield.

In this paper, we report the formation and the first isolation of cyclopropanol derivatives **4a–e**, the Favorskii-type intermediates in the reaction of cyclic α-halo ketones with sodiomalonates. Transformations of **4** to the corresponding ring-contracted β-keto esters **9a–d** and ketones **11a–d** are also described.

The structure of the bicyclo[3.1.0]hexane skeleton of **4c** was elucidated by spectral data and chemical transformations to known compounds, such as ethyl β-oxocyclopentanepropanoate (**9c**), cyclopentyl methyl ketone (**11c**), and 1-cyclopentenyl methyl ketone (**15**). The IR spectrum of **4c** showed a strong absorption of a hydroxyl group at 3500 cm^{-1}. The ^1H NMR spectrum exhibited a singlet (1 H) at δ 2.91 due to the α-H of the malonate moiety and the ^{13}C NMR spectrum indicated a signal at 29.8 ppm. This was split into a doublet (off-resonance decoupling) due to the two equivalent angular methine carbons. In the mass spectrum, a molecular ion peak was observed at *m/e* 256.

A conceivable mechanism for this reaction is shown in Scheme I. It is reasonable to consider that malonate anion reacts as a base initially to produce an equilibrium mixture

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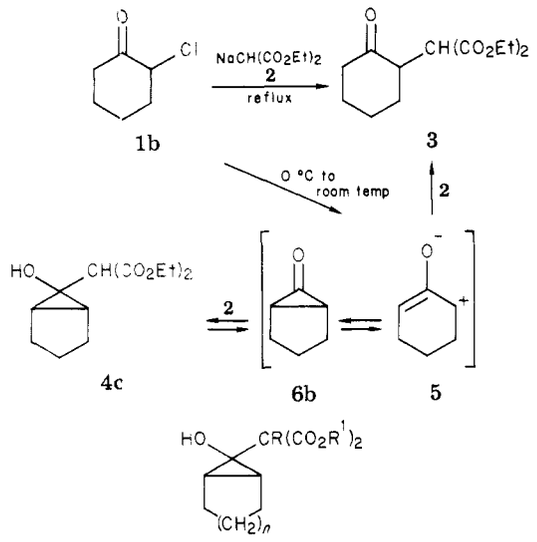
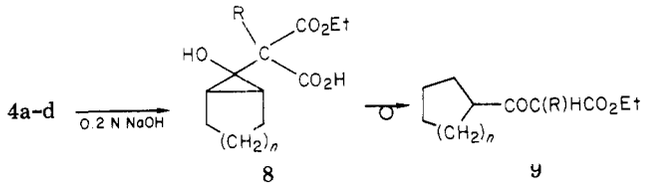
0022-3263/80/1945-0043$01.00/0

Scheme I



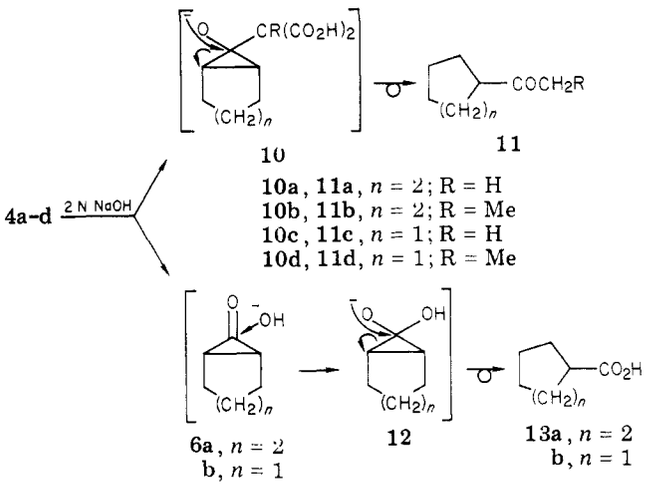
4a, n = 2; R = H; R^1 = Et
b, n = 2; R = Me; R^1 = Et
d, n = 1; R = Me; R^1 = Et
e, n = 1; R = H; R^1 = Me

Scheme II



8a, 9a, n = 2; R = H
8b, 9b, n = 2; R = Me
8c, 9c, n = 1; R = H
8d, 9d, n = 1; R = Me

Scheme III

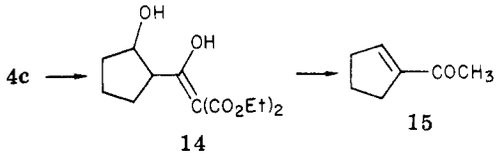


10a, 11a, n = 2; R = H
10b, 11b, n = 2; R = Me
10c, 11c, n = 1; R = H
10d, 11d, n = 1; R = Me

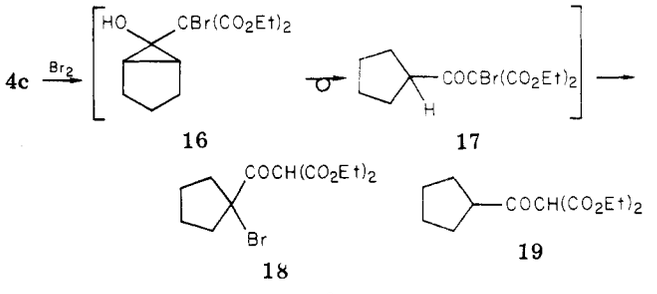
6a, n = 2
b, n = 1

13a, n = 2
b, n = 1

Scheme IV



Scheme V



of zwitterion **5** and cyclopropanone **6b** intermediates, which have been suggested to be involved in Favorskii rearrangement.[6]

Bicyclo compound **4c** was converted into **3** by heating in benzene at reflux temperature in the presence of NaH (0.05 equiv) in 85% yield. When the 1:1 mixture of **4c** and methyl malonate was heated with NaH (0.05 equiv) in benzene at reflux temperature, it was transformed into a mixture (29:31:39) of the ester **3**, methyl *C*-(2-oxocyclohexyl)malonate (**7**), and ethyl malonate as the result of the malonate moiety exchange.[7] These results suggest that under reflux conditions, ethyl malonate may be readily liberated from **4c** to regenerate intermediates **5** and **6b** in equilibrium, **5** being attacked by ethyl malonate or methyl malonate anions in competition to afford **3** and **7**, respectively.

Bicyclo compounds **4a**, **4b**, **4d**, and **4e** were prepared in 42–62% yields by the similar treatment of 2-chlorocycloheptanone (**1a**) or **1b** with the corresponding malonate anions. The ^{1}H NMR and IR spectral data of **4** are summarized in Table I and ^{13}C NMR spectral data are in Table II. When the reaction of **1b** with ethyl *C*-methylmalonate was done in dry THF, the yield of **4d** increased to 71%.[8] These bicyclo compounds are stable enough to be isolable by quick vacuum distillation[9] and/or column chromatography on silica gel.

The hydrolysis of **4a–d** with 0.2 N NaOH gave esters **8a–d**. Compounds **8a** and **8b** were used for the next steps without isolation because of their lability. Compound **8d** could be isolated as a crystal, mp 100–101 °C, in 78% yield. Pyrolysis of **8a–d** at 110–120 °C afforded β-keto esters **9a–d** in good yields.

The hydrolysis of **4** with 2 N NaOH gave dicarboxylic acids **10a–d**, which were allowed to be pyrolyzed without isolation to give ketones **11a–d** in 55–74% yields. Ring-contracted carboxylic acids **13a** and **13b** were obtained occasionally in 5–7% yields as byproducts. The mechanism for the formation of these minor products is illustrated in Scheme III. In this condition, malonate may be partially liberated by retrograde aldol reaction to produce cyclopropanone intermediate **6**, which is then converted into **13** via the known Favorskii mechanism. The alkaline hydrolysis in aqueous EtOH (4:1 H_2O–EtOH) gave only **11d** in 73% yield.

Treatment of **4c** with CrO_3 and $HClO_4$[10] caused the oxidative ring contraction to afford ethyl *C*-(2-hydroxycyclopentanecarbonyl)malonate (**14**) in 45% yield. It was transformed into **15**[11] in 23% yield by heating in Me_2SO in the presence of a catalytic amount of NaCl.[12]

(6) N. J. Turro and W. B. Hammond, *J. Am. Chem. Soc.*, **87**, 3258 (1965).
(7) There is no possibility of forming **7** by transesterification in this reaction, since the treatment of the ester **3** and methyl malonate under similar conditions only resulted in the recovery of **3**.
(8) The use of a twofold equivalent of malonate did not effect an increase of the yield.
(9) Prolonged heating in distillation caused the ring contraction to give compounds such as **9c** and **19**.
(10) A. M. Martinez, G. E. Cushmac, and J. Rocek, *J. Am. Chem. Soc.*, **97**, 6502 (1975).
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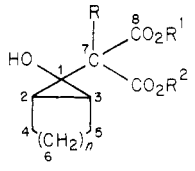
Table I. ^{1}H NMR ($CDCl_3$, δ) and IR (cm^{-1}) Spectral Data of Bicyclo Compounds 4a-e and 8c,d

	^{1}H NMR					
	ester					
compd	CH_3 (t, J = 7 Hz)	CH_2 (q, J = 7 Hz)	ring H (m)	R (s)	OH, CO_2H (br s)	IR
4a	1.27	4.21	0.75-1.0 1.2-2.2	2.83	3.46	3500, 1730
4b	1.26	4.17	0.85-1.05 1.2-2.2	1.32	3.40	3500, 1730
4c	1.27	4.21	1.3-2.2	2.91	3.53	3500, 1730
4d	1.25	4.15	1.0-2.1	1.38	3.35	3520, 1720
4e	3.78		1.3-2.1	2.95	3.45	3500, 1730
8c	1.29	4.20	1.5-2.2	2.86	6.66	3500, 3500-2500, 1725
8d[a]	1.25	4.16	1.5-2.1	1.41	4.92	3500, 3500-2500, 1710

[a] In CD_3COCD_3.

Table II. ^{13}C NMR Spectra ($CDCl_3$, ppm) of Bicyclo Compounds 4a-e and 8a,b



								R', R²	
compd	C-1 (s)	C-2,3 (d)	C-4,5 (t)	C-6 (t)	C-7	R (q)	C-8 (s)	CH_2 (t)	CH_3 (q)
4a	58.5	17.7	17.6	21.7	60.2 (d)		169.2	61.5	14.1
4b	60.9	17.7	17.4	21.8	60.1 (s)	14.5	172.3	61.5	14.1
4c	61.5	29.8	25.7	25.9	59.1 (d)		168.7	61.4	14.7
4d	62.0	27.3	25.6	26.6	59.8 (s)	18.1	171.7	61.4	13.9
4e	61.6	30.0	25.7	25.7	59.0 (d)		169.4		52.6
8c	61.7	30.0 30.1	25.7	25.7	59.1 (d)		169.0 172.1	61.8	14.0
8d[a]	63.5	27.1 27.4	25.9	26.4	59.6 (s)	17.9	176.0 171.7	61.9	13.9

[a] In CD_3COCD_3.

Treatment of **4c** with an equimolar amount of Br_2 at 50 °C gave a mixture of bromide **18** (67% yield) and compound **19** (10% yield). The off-resonance decoupled ^{13}C NMR spectrum of CBr in **18** showed a singlet. It may be suggested that in the formation of **18** bromide **16** can be an initial intermediate, which undergoes rearrangement to **17** followed by 1,3-migration of Br.[13] Compound **19** can be obtained directly from **4c** under acidic conditions.

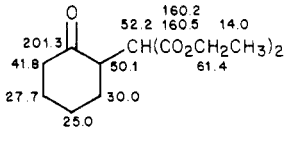
The present Favorskii-type reaction provides a useful and novel preparative way for β-keto esters and the corresponding ketones. Attempts to extend this procedure to other carbanions such as cyanoacetate[14] and acetoacetate[5] and to other α-halo cycloalkanones such as 2-chlorocyclopentanone (**20**),[15] 2-chloro-2-(ethoxycarbonyl)cyclohexanone (**21**),[16] and 6-bromo-2-(ethoxycarbonyl)cyclohexanone (**22**)[16] have not been successful so far, affording only S_N2 products.

Experimental Section

The melting points were determined on a Yamato Model MP-21 melting point apparatus and are uncorrected. The elemental analyses were carried out in our laboratory. The evaporative bulb-to-bulb distillations were done by using a Büchi Kugelrohrofen at the pressure and oven temperature indicated. IR spectra were determined on a Hitachi Model EPI-S2 spectrometer, mass spectra were obtained at 70 eV with a Hitachi Model RMS-4 mass spectrometer, and ^{1}H NMR spectra were determined at 60 MHz with a Hitachi Model R-24 spectrometer. Both ^{1}H NMR (100 MHz) and ^{13}C NMR[17] (25 MHz) spectra ($CDCl_3$) were taken on a JEOL Model FX-100 spectrometer equipped with FT facilities and using Me_4Si as an internal standard. The analytical determination by GLC was performed on a Hitachi Model K-53 gas chromatograph. Analytical and preparative TLCs were done on a silica gel (Kieselgel 60 PF_{254}, Merck A.G., Darmstadt) with layers of 0.25- and 1.0-mm thickness, respectively. Column chromatography was done on a silica gel (Wakogel C-200, Wako Junyaku Kogyo Co. Ltd.).

Starting materials such as **1a**,[18] **1b**,[18] **20**,[18] **21**,[11] and **22**[19] were prepared by procedures similar to those described in the literature.

Ethyl *C*-(2-Oxocyclohexyl)malonate (3) was obtained from the reaction of equimolar amounts of 2-chlorocyclohexanone and ethyl sodiomalonate in benzene under the conditions described in the literature:[3,4] yield 45% (lit.[3] yield 48%); bp 147 °C (6 mm); IR (neat) 1740, 1720 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.50–2.60 (m, 8 H, ring proton), 2.95–3.45 (m, 1 H, α-methine proton of ring), 3.64 (d, 1 H, J = 10 Hz, $CH(CO_2Et)_2$), 4.18 (q, 4 H, J = 7 Hz, ester 2 CH_2). The ^{13}C NMR spectrum (ppm) is summarized in the following:



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(13) A. Svendsen and P. M. Boll, *Tetrahedron*, **29**, 4251 (1973).
(14) B. Belleau, *Can. J. Chem.*, **35**, 651 (1957).
(15) M. H. Khorgami, *Q. Bull. Fac. Sci., Tehran Univ.*, **2**, 19 (1971); *Chem. Abstr.*, **75**, 63519 (1971).
(16) Laboratory work by Mr. Junichi Tanabe. Axially fixed halogen tends to retard the Favorskii-type rearrangement: H. O. House and H. W. Thompson, *J. Org. Chem.*, **28**, 164 (1963).
(17) The pulse width was 4 μs (30° TIP) and FIDs were compiled by using 8K data points over a spectral width of 6000 Hz. The off-resonance decoupling was used to support the assignment.
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Typical Reaction for the Synthesis of Bicyclo[3.1.0]hexan-6-ol and Bicyclo[4.1.0]heptan-7-ol. 6-[Bis(ethoxycarbonyl)methyl]bicyclo[3.1.0]hexan-6-ol (4c). A mixture of Na (0.45 g, 0.02 g-atom) and ethyl malonate (3.17 g, 0.02 mol) in 15 mL of benzene was heated under reflux for 8 h until the Na turnings were completely dissolved. After the mixture was cooled to 0 °C, 2-chlorocyclohexanone (3.15 g, 0.024 mol) was added dropwise. The mixture was stirred for 2 h at 0 °C and for an additional 6 h at room temperature (25 °C). The resulting mixture was acidified with 10% HCl. The aqueous layer was extracted with ether and the combined organic layers were washed with water and dried over $MgSO_4$. The removal of the solvent left 3.95 g of yellow oil, which was subjected to quick distillation to give 2.55 g of bicyclohexanol **4c** (49% yield), bp 110–120 °C (4 mm). The analytical sample was obtained by column chromatography on silica gel (10:1 hexane–acetone) and subsequent bulb-to-bulb distillation: MS m/e (relative intensity) 256 (M^+, 2), 211 (M – OEt, 3), 187 (12), 183 (M – CO_2Et, 12), 182 (18), 165 (28), 161 (56), 160 ($CH_2(CO_2Et)_2$, 100), 133 (79), 96 (86).

Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.84. Found: C, 60.82; H, 7.58.

7-[Bis(ethoxycarbonyl)methyl]bicyclo[4.1.0]heptan-7-ol (4a): yield 52%; bp 145–160 °C (2 mm); MS m/e (relative intensity) 270 (M^+, 2), 252 (M – H_2O, 1), 225 (M – OEt, 5), 197 (M – CO_2Et, 16), 179 (39), 160 ($CH_2(CO_2Et)_2$, 74), 133 (100), 115 (99), 110 (98), 87 (91).

Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.43; H, 8.24.

7-[1,1-Bis(ethoxycarbonyl)ethyl]bicyclo[4.1.0]heptan-7-ol (4b): yield 62%; bp 155–167 °C (2 mm); MS m/e (relative intensity) 284 (M^+), 266 (M – H_2O), 238 (2), 211 (M – CO_2Et, 6), 210 (5), 174 ($CH_3CH(CO_2Et)_2$, 71), 128 (100), 100 (56), 67 (76).

Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.03; H, 8.22.

6-[1,1-Bis(ethoxycarbonyl)ethyl]bicyclo[3.1.0]hexan-6-ol (4d): yield 42%; bp 130–135 °C (3 mm); MS m/e (relative intensity) 224 (M – EtOH), 174 (66), 151 (23), 128 (100), 100 (76), 83 (73).

Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 61.85; H, 8.40.

6-[Bis(methoxycarbonyl)methyl]bicyclo[3.1.0]hexan-6-ol (4e): yield 47%; bp 131–137 °C (6 mm); MS m/e (relative intensity) 228 (M^+, 0.4), 210 (M – H_2O, 2), 169 (M – OEt, 5), 132 ($CH_2(CO_2Me)_2$, 37), 101 (47), 100 (38), 96 (53), 69 (100).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 58.27; H, 7.14.

Base-Catalyzed Conversion of 4c into 3. A mixture of cyclopropanol **4c** (263 mg, 1.02 mmol) and NaH (1.2 mg, 0.051 mmol) in 5 mL of dry benzene was heated under reflux for 5 h. After cooling, the mixture was acidified with 2 mL of 10% HCl. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was treated in a usual manner to give 225 mg of the product **3** (85% yield) by vacuum distillation.

This reaction was carried out under a variety of reaction times. The reaction times and products (yields determined by ^1H NMR) were as follows: 1 h, **3** (78%) and **4c** (12%); 15 min, **3** (66%) and **4c** (34%).

Base-Catalyzed Reaction of 4c and Methyl Malonate. A mixture of **4c** (1.02 g, 4 mmol), methyl malonate (0.53 g, 4 mmol), and NaH (5 mg, 0.2 mmol) in 10 mL of benzene was heated under reflux for 3.5 h. After cooling, the mixture was treated in the way described in the preceding experiment to give 1.52 g of yellow oil. It was subjected to distillation to give two fractions: The first fraction (bp 90–120 °C (50 mm), 0.53 g) was an equiamount mixture of ethyl malonate (46% yield from **4c**) and methyl malonate. Preparative TLC (3:1 hexane–acetone) on a silica gel of the second fraction (bp 130–150 °C (3 mm)), gave **3** and **7** in 35% and 37% yields, respectively. **7**: IR (neat) 1730, 1705 (C=O) cm^{-1}; ^1H NMR (CCl_4) δ 1.30–2.50 (m, 9 H, ring proton), 3.52 (d, 1 H, J = 10 Hz, α-H of esters), 3.66 (s, 6 H, ester 2 CH_3).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.62; H, 7.15.

Ethyl *C*-(2-Oxocyclopentyl)malonate. A similar treatment of equimolar amounts of 2-chlorocyclopentanone **20** and ethyl sodiomalonate in benzene as described above gave only ethyl *C*-(2-oxocyclopentyl)malonate in 51% yield: bp 130–150 (7 mm); IR (neat) 1730 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (dt, 6 H, J = 7 Hz, 2 CH_3, 1.4–2.9 (m, 7 H, ring proton), 3.75 (d, 1 H, J = 5 Hz, α-H of esters), 4.15 (dq, 4 H, J = 7 Hz, ester 2 CH_2).

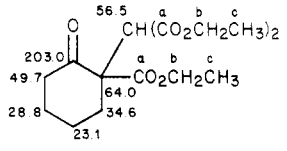
Ethyl α-cyano-2-oxocyclohexaneacetate: yield 32%, bp 130–140 °C (1 mm); ^1H NMR ($CDCl_3$) δ 1.31 (t, 3 H, J = 7 Hz, ester CH_3), 1.4–2.7 (m, 8 H, ring proton), 2.8–3.3 (m, 1 H, ring CH), 4.00 (d, 1 H, J = 7 Hz, α-H of ester), 4.27 (q, 2 H, J = 7 Hz, ester CH_2). The IR spectrum was identical with that described in the literature.[14]

Ethyl α-acetyl-2-oxocyclohexaneacetate: yield 31%; bp 129–145 °C (2 mm); IR (neat) 1750, 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, 3 H, J = 7 Hz, ester CH_3), 0.9–2.6 (m, 8 H, ring proton), 2.27 (s, 1.2 H) and 2.32 (s, 1.8 H) ($COCH_3$), 3.0–3.6 (m, 1 H, ring CH), 3.80 (d, 1 H, J = 10 Hz, α-H of ester), 4.17 (q, 2 H, J = 7 Hz, ester CH_2).

Ethyl *C*-[1-(Ethoxycarbonyl)-2-oxocyclohexyl]malonate. A similar reaction of 2-chloro-2-(ethoxycarbonyl)cyclohexanone with ethyl sodiomalonate (1:1) in THF for 35 h at room temperature gave a viscous oil, bp 125–200 °C (0.4 mm). TLC (3:1 hexane–acetone) showed three main spots at R_f 0.61, 0.50, and 0.30 in the ratio of 1.3:1.0:0.4 (w/w), respectively. Preparative TLC gave ethyl *C*-[1-(ethoxycarbonyl)-2-oxocyclohexyl]malonate in 15% yield: R_f 0.50; IR (neat) 1735 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21, 1.26, and 1.27 (t, respectively, 9 H, ester 3 CH_3), 3.58 and 3.62 (s, respectively, 1 H, α-H of esters), 4.04–4.35 (m, 6 H, ester 3 CH_2); MS m/e (relative intensity) 328 (M^+), 299 (M – Et), 283 (M – OEt), 255 (M – CO_2Et), 211 (21), 165 (40), 138 (91), 111 (68), 93 (77), 65 (100).

Anal. Calcd for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.50; H, 7.53.

The ^{13}C NMR spectrum (ppm) is summarized in the following:



a, 171.8, 170.7, 167.4
b, 62.0, 61.7, 61.3
c, 14.0, 13.8

The structures of the compounds with R_f 0.61 and 0.30 were not elucidated.

Ethyl *C*-[3-(ethoxycarbonyl)-2-oxocyclohexyl]malonate was obtained in 19% yield by a similar reaction of 6-bromo-2-(ethoxycarbonyl)cyclohexanone with ethyl sodiomalonate (1:1): bp 140–165 °C (0.23 mm); IR (neat) 1735 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (t, 9 H, ester CH_3), 1.57–2.74 (m, 7 H, ring proton), 3.7–4.0 (m, 1.9 H, α-H of esters), 4.32 (q, 6 H, ester 3 CH_2), 12.45 (s, 0.1 H, enol OH).

Anal. Calcd for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.65; H, 7.33.

Typical Procedure for the Hydrolysis of 4a-d with 0.2 N NaOH. 6-[1-Carboxy-1-(ethoxycarbonyl)ethyl]bicyclo-[3.1.0]hexan-6-ol (8d). The suspension of bicyclohexanol **4d** (1.0 g, 3.7 mmol) in 25 mL of 0.2 N NaOH was stirred for 20 h at room temperature. The unreacted **4d** was removed by extraction with ether. After being acidified (10% HCl), the aqueous layer was extracted with ether. Removal of the solvent after drying over $MgSO_4$ left 715 mg of crystalline acid ester **8d**, yield 78%. The analytical sample was obtained by one recrystallization from benzene–hexane (1:1): mp 100–101 °C dec; MS m/e (relative intensity) 198 (M – CO_2, 0.2), 152 (11), 125 (M – CO_2 – CO_2Et), 102 (18), 97 ($C_5H_9CO^+$, 57), 69 ($C_5H_9^+$, 100).

Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.75; H, 7.69.

6-[Carboxy(ethoxycarbonyl)methyl]bicyclo[3.1.0]hexan-6-ol (8c). The hydrolysis of **4c** with 0.2 N NaOH gave a viscous oil of **8c**, yield 60%. It was not stable enough to get an acceptable elemental analysis.

Typical Procedure for Thermal Rearrangement of Acid Esters 8a–d to β-Keto Esters 9a–d. Ethyl β-Oxocyclopentanepropanoate (9c). Acid ester **8c** (200 mg, 0.0887 mmol) was heated at 110 °C until evolution of carbon dioxide ceased. The resulting yellow oil was subjected to distillation to give 160

mg of **9c**: yield 99%; bp 90–95 °C (1 mm). The IR and ^{1}H NMR spectra were identical with those described in the literature.[20]

Ethyl α-methyl-β-oxocyclopentanepropanoate (9d) was obtained similarly by the thermal rearrangement of **8d**: yield 86%; bp 95–115 °C (1 mm); IR (neat) 1743, 1714 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, 3 H, J = 7 Hz, ester CH_3), 1.33 (d, 3 H, J = 7 Hz, α-CH_3), 1.5–2.2 (m, 8 H, ring proton), 3.02 (m, 1 H, ring CH), 3.60 (q, 1 H, J = 7 Hz, α-H), 4.15 (q, 1 H, J = 7 Hz, ester CH_2); MS m/e (relative intensity) 198 (M^+, 1), 153 (M – EtO, 2), 129 (M – C_5H_9, 4), 97 ($C_5H_9CO^+$, 80), 69 (C_5H_9, 100).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.52; H, 9.24.

Ethyl β-Oxocyclohexanepropanoate (9a). Hydrolysis of **4a** with 0.2 N NaOH followed by the pyrolysis of the resulting acidic oil gave β-keto ester **9a**: yield 65%; bp 145–165 °C (20 mm). The IR and ^{1}H NMR spectra were identical with those of an authentic sample.[20]

Ethyl α-methyl-β-oxocyclohexanepropanoate (9b) was obtained similarly from **4b**: yield 55%; bp 145–165 °C (20 mm); IR (neat) 1710, 1735 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, 3 H, J = 7 Hz, ester CH_3), 1.31 (d, 3 H, J = 7 Hz, α-CH_3), 1.0–2.1 (m, 10 H, ring proton), 2.50 (m, 1 H, ring CH), 3.64 (q, 1 H, J = 7 Hz, α-H), 4.14 (q, 2 H, J = 7 Hz, ester CH_2); MS m/e (relative intensity) 212 (M^+), 167 (M – OEt, 2), 127 (M – C_6H_{11}, 6), 111 (33), 83 (C_6H_{11}, 100).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.76; H, 9.32.

Transformation of 4a–d to Ketones 11a–d. Cyclopentyl Methyl Ketone (11c). The following experiment illustrates the manner in which **11** was prepared from **4**. A suspension of **4c** (1.0 g, 3.9 mmol) in 80 mL of 2 N NaOH was stirred for 24 h at room temperature. The mixture was treated with ether to remove the unreacted **4c**. The aqueous layer was acidified (10% HCl) and then extracted with ether. Removal of the solvent left 425 mg of oil, which was subjected to fractional distillation to give 244 mg of ketone **11c** (56% yield) and 23 mg of cyclopentanecarboxylic acid (**13b**) (5% yield). The acid **13b** was converted into its methyl ester[21] (CH_2N_2), which was identified by IR, ^{1}H NMR, and GLC analysis. Ketone **11c**: bp 120–145 °C (90 mm); ^{1}H NMR ($CDCl_3$) δ 1.22–2.20 (m, 8 H, ring proton), 2.15 (s, 3 H, CH_3), 2.84 (m, 1 H, ring CH). Semicarbazone of **11c**: mp 145.5–146 °C (lit.[22] mp 142–143 °C). The IR spectrum of **11c** was identical with that of an authentic sample.[23]

Cyclohexyl methyl ketone (11a):[23] yield 74%; bp 135–150 °C (20 mm); IR (neat) 1710 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8–2.0 (m, 10 H, ring proton), 2.10 (s, 3 H, CH_3), 2.35 (m, 1 H, ring CH). Cyclohexanecarboxylic acid (**13a**) was produced in 7% yield as a byproduct.

Cyclohexyl ethyl ketone (11b):[24] yield 61%; bp 155–160 °C (20 mm); IR (neat) 1710 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_3), 0.8–2.0 (m, 10 H, ring proton), 2.30 (m, 1 H, ring CH), 2.40 (q, 2 H, J = 7 Hz, CH_2). Compound **13a** was produced in 5% yield.

Cyclopentyl ethyl ketone (11d):[24] yield 55%; bp 120–130 °C (25 mm); IR (neat) 1705 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.04 (t, 3 H, J = 7 Hz, CH_3), 1.3–2.2 (m, 8 H, ring proton), 2.47 (q, 2 H, J = 7 Hz, CH_2CH_3), 2.87 (m, 1 H, ring CH). Compound **13b** was obtained in 5% yield.

Pyrolysis of 4c. Bicyclo compound **4c** (918 mg, 3.76 mmol) was heated at 300 °C for 1 h. Vacuum distillation of the resulting mixture gave 360 mg (52% yield) of **9c**, bp 65–87 °C (9 mm).

Ethyl C-(2-Hydroxycyclopentanecarbonyl)malonate (14). To a stirred suspension of CrO_3 (398 mg, 3.2 mmol) in 4 mL of aqueous AcOH (1:1 (v/v)) were added successively 3 mL of 60% aqueous $HClO_4$ and a solution of **4c** (1.28 g, 5 mmol) in 1 mL of AcOH dropwise at 0 °C. After 6 h of stirring at 0 °C, the mixture was poured into ice-cold water. The organic layer was extracted with ether, washed with aqueous $NaHCO_3$ and brine, and dried over $MgSO_4$. Removal of the solvent left 839 mg of a brown oil, which was subjected to TLC (3:1 hexane–acetone) analysis, showing two main spots at R_f 0.28–0.39 and 0.13, representing **4c** (35%) and **14** (57%; 45% yield on the basis of consumed **4c**), respectively. The analytical sample of **14** was obtained by column chromatography on silica gel (Wakogel C-200, 10:1 hexane–acetone): IR (neat) 3450 (OH), 1725 (ester C=O), 1635 (enol C=C) cm^{-1}; ^{1}H NMR (CCl_4) δ 1.31 (dt, 6 H, J = 7 Hz, ester 2 CH_3), 1.4–2.6 (m, 6 H, ring proton), 2.90 (m, 1 H, C_1–H), 4.21 (dq, br s, 5 H, J = 7 Hz, ester 2 CH_2 and C(OH)**H**), 4.60 (s, 1 H, OH), 13.5 (br s, 1 H, enol OH); MS m/e (relative intensity) 254 (M – H_2O), 182 (2), 160 (2), 136 (4), 115 (9), 110 (100), 95 ($C_5H_7CO^+$, 100).

Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.24. Found: C, 57.60; H, 7.15.

1-Cyclopentenyl Methyl Ketone (15). A mixture of **14** (378 mg, 37 mmol) and NaCl (66 mg) in 3 mL of Me_2SO was heated at 120–150 °C until evolution of gas ceased. After addition of 10 mL of H_2O, the organic layer was extracted with ether, washed with water, and dried over $MgSO_4$. Removal of the solvent left 35 mg (23% yield) of **15**. The IR and ^{1}H NMR spectra were identical with those described in the literature.[11]

Ethyl C-(1-Bromocyclopentanecarbonyl)malonate (18). To the solution of **4c** (1.28 g, 5 mmol) in 30 mL of CCl_4 was added bromine (0.8 g, 5 mmol) dropwise at 0 °C. After 45 min of stirring at 50 °C, the mixture was poured into 10 mL of water. Workup carried out in a usual manner gave 1.63 g of yellow oil. Separation by column chromatography on silica gel (20 g of Wakogel C-200, 10:1 hexane–acetone) gave 1.08 g of **18** (64% yield) and 0.12 g of ethyl C-cyclopentanecarbonylmalonate (**19**) (10% yield). Analytical samples of **18** and **19** were obtained by bulb-to-bulb distillations.

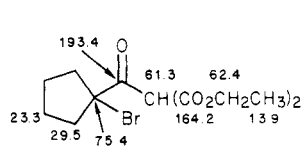
18: bp 120–150 °C (1 mm); IR (neat) 1730, 1710 (C=O) cm^{-1}; ^{1}H NMR (CCl_4) δ 1.30 (t, 6 H, J = 7 Hz, ester 2 CH_3), 1.5–2.7 (m, 8 H, ring proton), 4.21 (q, 4 H, J = 7 Hz, ester 2 CH_2), 5.09 (s, 1 H, α-H of esters).

Anal. Calcd for $C_{13}H_{19}O_5Br$: C, 46.61; H, 5.73. Found: C, 46.72; H, 5.81.

19: bp 120–130 °C (1 mm); IR (neat) 1750–1720 (C=O), 1640, 1600 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (dt, 6 H, ester 2 CH_3), 1.4–2.5 (m, 8 H, ring proton), 3.0 (m, 1 H, ring CH), 3.95–4.45 (m, 4.75 H, ester 2 CH_2 and keto form α-H of ester), 13.34 (br s, 0.25 H, enol OH).

Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.75; H, 7.65.

The ^{13}C NMR spectrum (ppm) of **18** is summarized in the following:



Registry No. 1b, 822-87-7; **2**, 996-82-7; **3**, 4039-31-0; **4a**, 71911-60-9; **4b**, 71911-60-9; **4c**, 71911-61-0; **4d**, 71911-62-1; **4e**, 71911-63-2; **7**, 63965-89-9; **8c**, 71911-64-3; **8d**, 71911-65-4; **9a**, 15971-92-3; **9b**, 71911-66-5; **9c**, 24922-00-7; **9d**, 71911-67-6; **11a**, 5664-21-1; **11b**, 1123-86-0; **11c**, 6004-60-0; **11d**, 6635-67-2; **13a**, 98-89-5; **13b**, 3400-45-1; **14**, 71911-68-7; **15**, 16112-10-0; **18**, 71911-69-8; **19**, 71911-70-1; **20**, 694-28-0; methyl malonate, 108-59-8; ethyl C-(2-oxocyclopentyl)malonate, 32923-03-8; ethyl α-cyano-2-oxocyclohexaneacetate, 71911-71-2; ethyl α-acetyl-2-oxocyclohexaneacetate, 71911-72-3; ethyl C-(1-ethoxycarbonyl-2-oxocyclohexyl)malonate, 71911-73-4; 2-chloro-2-(ethoxycarbonyl)cyclohexanone, 71911-74-5; ethyl C-[(3-ethoxycarbonyl)-2-oxocyclohexyl]malonate, 71911-75-6; 6-bromo-2-(ethoxycarbonyl)cyclohexanone, 30132-23-1.

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