Oxidation of Ethyl *trans*- and *cis*-3-Bromo-1-methyl-2-oxocyclohexanecarboxylates by Dimethyl Sulphoxide

By **Kikumasa Sato,* Seiichi Inoue,** and **Masao Hirayama,** Department of Applied Chemistry, Faculty of Engineering, Yokohama National University, Ooka, Minami-ku, Yokohama 233
Masao Ōhashi, Chemical Laboratory, Seimi Chemical Co., Ltd., Chigasaki, Chigasaki-shi, Kanagawa 253, Japan

Ethyl *c*-3-bromo-1-methyl-2-oxocyclohexane-*r*-1-carboxylate (1a) is oxidized by dimethyl sulphoxide to the 2,3-dione derivative (3), whereas the *t*-3-bromo-isomer (1b) is apparently dehydrogenated to give the bromocyclohexenone (4). The mechanism for the formation of the product (4) is discussed. Allied reactions are described.

KORNBLUM [1] found that phenacyl bromides can be oxidized to glyoxals by treatment with dimethyl sulphoxide (DMSO). Iacona *et al.*[2] reported that treatment of methyl 4β-bromo-3-oxo-5β-cholan-24-oate with DMSO in the presence of sodium hydrogen carbonate gave the corresponding α-diketone together with a dehydrobrominated compound.

We have described the oxidation of 2-bromocycloalkanones by DMSO to give solely 3-bromo-2-hydroxycycloalk-2-enones;[3] however we obtained 2-hydroxycycloalk-2-enones when this oxidation was carried out in the presence of epichlorohydrin as a scavenger for hydrogen bromide. During our studies on the synthesis of α-diketones we found that oxidation of ethyl *c*-3-bromo-1-methyl-2-oxocyclohexane-*r*-1-carboxylate (1a) in the presence of epichlorohydrin at 70 °C afforded ethyl 3-hydroxy-1-methyl-2-oxocyclohex-3-enecarboxylate along with its 4-bromo-derivative (3); we considered that the latter product (3) was derived from an initially formed α-diketone and bromine produced *in situ*.[4] However, the *t*-3-bromo-ester (1b) treated simil-

[1] N. Kornblum, *J. Amer. Chem. Soc.*, 1957, **76**, 6562.
[2] R. N. Iacona, A. T. Rowland, and H. R. Nace, *J. Org. Chem.*, 1964, **29**, 3495.
[3] K. Sato, S. Suzuki, and Y. Kojima, *J. Org. Chem.*, 1967, **32**, 339; K. Sato, Y. Kojima, and H. Sato, *ibid.*, 1970, **35**, 2374.
[4] K. Sato, S. Inoue, and M. Ōhashi, *Bull. Chem. Soc. Japan*, 1974, **47**, 2519.

arly, was unchanged. We were interested to know why the reactivities of (1a and b) toward DMSO were different, and now the results of reactions in the absence of a scavenger for hydrogen bromide.

Although the bromination of ethyl 1-methyl-2-oxocyclohexanecarboxylate [5] has been shown to give the 3-bromo-derivative, no indication of the stereochemistry of the product was given. We reinvestigated this bromination using an equimolar amount of bromine in carbon tetrachloride or light petroleum, and obtained a liquid bromide (1a) directly in a pure state and in high yield. This underwent isomerization at room temperature in a few weeks to give a solid bromide (1b). This irreversible isomerization apparently proceeds *via* enolization of the ketone group.* The ethoxycarbonyl group in a cyclohexane ring is somewhat less bulky than a methyl group (free energy difference *ca.* 0.6 kcal mol^{-1}), and dipole interactions between the ketone function and the ethoxycarbonyl group might be expected further to destabilize an equatorial relative to an axial isomer.

I.r. and u.v. absorption maxima of the bromides (1a and b)

Compound	ν/cm^{-1} [a]	Shift ($\Delta\nu$/cm^{-1})	(EtOH) $\lambda_{max.}$/nm (ε) [b]
Ethyl 1-methyl-2-oxocyclohexanecarboxylate [c]	1 718		
(1a)	1 731	13	269 [d] (240)
(1b)	1 732	14	276 (62)
Ethyl 3,3-dibromo-1-methyl-2-oxocyclohexanecarboxylate	1 730	12	

[a] Determined on a Hitachi EPI-2 instrument equipped with a NaCl prism; 2% solutions in CCl_4; rock salt cell of 0.05 mm thickness. [b] Determined by Hitachi EPS-3T spectrophotometer; EtOH as solvent; concentration *ca.* 10^{-4}M. [c] S. J. Rhoads, J. C. Gilbert, A. W. Decola, T. R. Garland, R. J. Spangler, and M. J. Urbigkit, (*Tetrahedron*, 1963, **19**, 1625) report 1 719 cm^{-1}, and a favoured conformation with the ethoxycarbonyl group axial. [d] Lit.,[5e] 269 nm (ε 260).

For ethyl 3-bromo-1-methyl-2-oxocyclohexanecarboxylate there are four possible chair form isomers (Scheme 1). The n.m.r. spectra of the isomers obtained (1a and b), in carbon tetrachloride, indicated the equatorial orientation of the bromine atom in each case by the presence of an axial 3-proton signal [6] [(1a) multiplet, width 18.1 Hz, at δ 4.78; (1b) multiplet, width 18.1 Hz, at δ 4.68]. I.r. carbonyl absorptions (Table) agree with this assignment, by their high frequency shift.[5c,7] The u.v. spectra of the two isomers in ethanol differ in that (1b) shows a bathochromic shift of 7 nm, implying that the ethoxycarbonyl group is axially oriented.[8,†] From these results, the liquid bromide is the *c*-3-bromo-isomer (1a) (equatorial bromo and axial methyl group) and the solid bromide the *t*-3-bromo-isomer (1b) (equatorial bromo and equatorial methyl group).

Treatment of the bromide (1a) with DMSO at 70 °C for 8 h gave ethyl 4-bromo-3-hydroxy-1-methyl-2-oxocyclohex-2-enecarboxylate (3) (isolated in 60% yield), apparently derived from the initial α-diketone (2) and bromine formed *in situ*.[9] Under the same conditions, the bromide (1b) was unchanged. However (1b) in DMSO at a higher temperature (75—78 °C) for 20 h afforded ethyl 3-bromo-1-methyl-2-oxocyclohex-3-enecarboxylate (4) (30%) as the sole isolated product; no α-diketone derivative was isolated (Scheme 2).

Scheme 1

Scheme 2

Formation of the α-diketone (3) could proceed *via* the usual back-side nucleophilic attack at C-3 by DMSO, followed by conformational inversion to give axial bromine in the transition state. The resultant diketone would then give (3) by bromination due to bromine in the medium ($2HBr + DMSO \longrightarrow Br_2 + DMS + H_2O$) (Scheme 3).

* Isomerization of *trans*- to *cis*-2,6-dibromocyclohexanone has been observed at room temperature in our laboratory.

† The electronegativity of ethoxycarbonyl group is assumed to be identical with that of the bromine atom (G. E. K. Branch and M. Calvin, ' The Theory of Organic Chemistry; An Advanced Course,' Prentice-Hall Inc., New York, 1941, p. 146, Table 16).

[5] (*a*) N. A. Milas, U.S.P. 2 407 673/1946; (*b*) S. M. Mukherjee, *J. Indian Chem. Soc.*, 1948, **25**, 155; (*c*) S. Inayama, *Chem. and Pharm. Bull.* (*Japan*), 1956, **4**, 198; (*d*) M. Yanagita, S. Inayama, and R. Kitagawa, *J. Org. Chem.*, 1956, **21**, 612; (*e*) J. S. Moffatt, *J. Chem. Soc.*, 1960, 3045; (*f*) M. Protiva, J. O. Jilek, L. Novak, E. Adlerova, I. Simak, and E. Knobloch, *Chem. listy*, 1955, **49**, 1198.

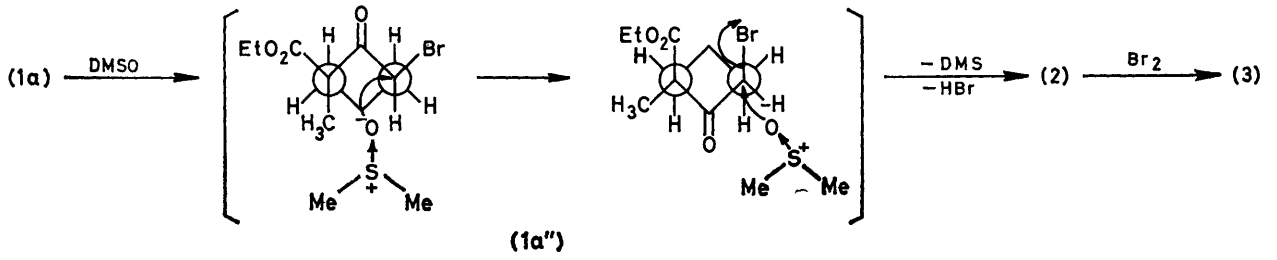
[6] E. W. Garbish, jun., *J. Amer. Chem. Soc.*, 1964, **86**, 1780.

[7] E. J. Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 3297.

[8] R. C. Cookson, *J. Chem. Soc.*, 1954, 282.

[9] I. M. Hunsberger and J. M. Tien, *Chem. and Ind.*, 1967, 88.

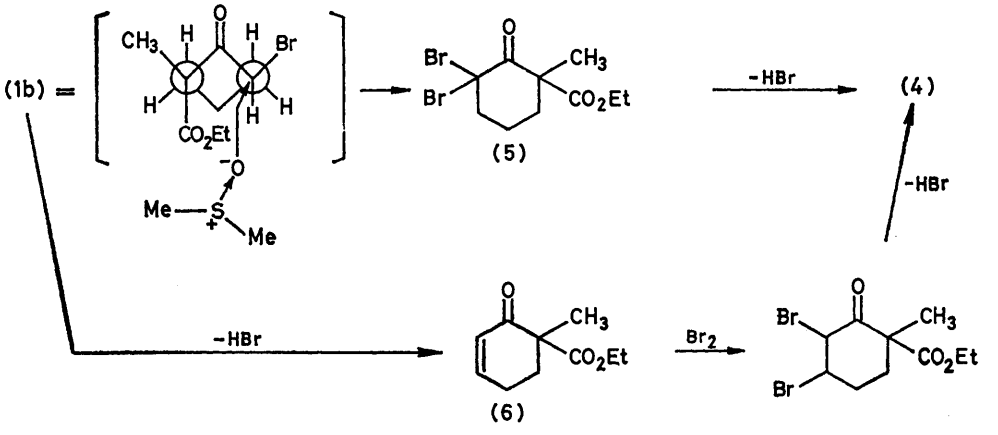
Possible routes to the product (4) are shown in Scheme 4. Nucleophilic attack at C-3 is hindered sterically and by the electronic repulsion of the axial ethoxycarbonyl group. The dibromide (5), produced by disproportionation or bromination, would easily suffer dehydrobromination to give (4) under the reaction conditions. The alternative pathway *via* the dehydrobrominated product (6) cannot be excluded [*cf.* the transformation of (16) to (17)]. As expected, treatment of ethyl 3,3-dibromo-1-methyl-2-oxocyclohexanecarboxylate (5) in DMSO at 75 °C for 8 h afforded (4) in high yield (92%). Compound (4) was also obtained (56%) from the reaction of ethyl 1-methyl-2-oxocyclohex-3-enecarboxylate (6) with 0.5 equiv. of bromine in DMSO at 70—75 °C for 8 h.



SCHEME 3

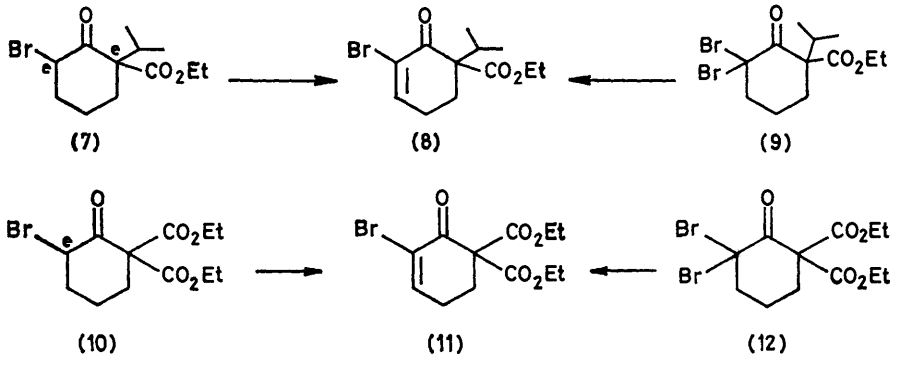
Similarly, treatment of ethyl 3-bromo-1-isopropyl-2-oxocyclohexanecarboxylate (7) [Br and Pr^i equatorial; the isomer corresponding to (1a) could not be isolated], the predominant product of bromination of ethyl 1-isopropyl-2-oxocyclohexanecarboxylate, afforded the dehydrogenation product (8); this compound was also obtained from dehydrobromination of ethyl 3,3-dibromo-1-isopropyl-2-oxocyclohexanecarboxylate (9).

We also examined the behaviour of DMSO towards diethyl 3-bromo-2-oxocyclohexane-1,1-dicarboxylate (10); only the dehydrogenation product (11) was obtained, in 64% yield. Compound (11) was identical with a sample prepared by dehydrobromination of diethyl 3,3-dibromo-2-oxocyclohexane-1,1-dicarboxylate (12).



SCHEME 4

Similar oxidation also occurred in the case of diethyl 3-bromo-2-oxocyclopentane-1,1-dicarboxylate (13) which could not eliminate hydrogen bromide: * the enone (14) was the only product obtained.



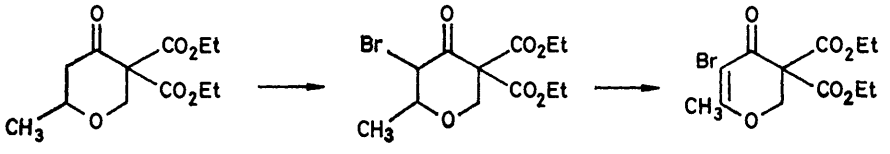
* Even when (13) was treated with quinoline at 150—160 °C, the dehydrobromination product was obtained in less than 10% yield.

The bromotetrahydropyran diester (16), prepared by bromination of the tetrahydropyran diester (15), also provided the dehydrogenation product (17) with DMSO.

(13) (14)

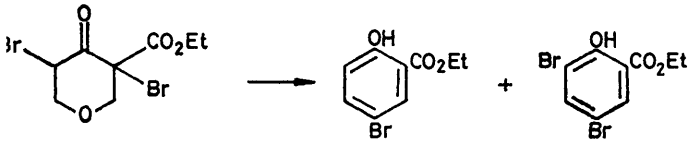
Attempted further bromination of (16) was unsuccessful.

Finally, we examined the effect of DMSO on ethyl 1,3-dibromo-2-oxocyclohexanecarboxylate (18),[10] which



(15) (16) (17)

is reported to be subject to dehydrobromination.[11] The products were ethyl 5-bromosalicylate (19) and ethyl 3,5-dibromosalicylate (20), obtained in moderate yield.



(18) (19) (20)

EXPERIMENTAL

I.r. spectra were recorded with a Hitachi 215 spectrophotometer, n.m.r. spectra with a JEOL C-60 spectrometer (tetramethylsilane as internal reference), and mass spectra with a Hitachi RMU-6L spectrometer. G.l.c. was performed with a ShimadzuGC-4A instrument [20% Silicone DC-200 on 60—80 mesh Cerite (3 m × 3 mm)]. For column chromatography Wakogel C-100 and C-200 (Wako Pure Chemical Industries) were used.

Ethyl c- *and* t-3-*Bromo*-1-*methyl*-2-*oxocyclohexane*-r-1-*carboxylates* (1a *and* b).—To a stirred solution of ethyl 1-methyl-2-oxocyclohexanecarboxylate (6.5 g) in carbon tetrachloride (90 ml), bromine (5.8 g) in carbon tetrachloride (10 ml) was added dropwise at 10 °C. The mixture was stirred for 4 h, then poured into water, and the organic layer was washed with aqueous sodium hydrogen carbonate and aqueous sodium chloride, dried ($MgSO_4$), and evaporated. Distillation of the residual oil gave the pure *bromide* (1a) (8.1 g, 88%), b.p. 102—103 °C at 0.7 mmHg (lit.,[5e] b.p. 127—128 °C at 2 mmHg), n_D^{20} 1.491 4, $\nu_{max.}$ (neat) 1 730 (ester C=O) and 1 712 cm^{-1} (ketone C=O), $\lambda_{max.}$ (EtOH) 269 nm (ε 240) [lit.,[5e] 269 nm (ε 260)], δ (CCl_4) 1.28 (3 H, d, *J* 7.0 Hz, Me), 1.32 (3 H, s, ring Me), 1.6—2.7 (6 H, m, ring protons), 4.23 (2 H, q, *J* 7.0 Hz, OCH_2), and 4.78 (1 H, m, width 18.1 Hz) (Found: C, 45.6; H, 5.8; Br, 30.1. $C_{10}H_{15}BrO_3$ requires C, 45.6; H, 5.75; Br, 30.3%), >99% pure by g.l.c. immediately after distillation.

The liquid bromide was set aside for several weeks at room temperature; the solid bromide was precipitated. Filtration and recrystallization from light petroleum gave (1b) as *needles*, m.p. 49.0—49.5 °C (lit.,[5e] 50—51 °C), >99.5% pure by g.l.c. on Silicone DC-200 (200 °C; 1.9 kg cm^{-2} He; t_R 7.5 min), $\nu_{max.}$ (KBr) 1 730 (ester C=O) and 1 714 cm^{-1} (ketone C=O), $\lambda_{max.}$ (EtOH) 276 nm (ε 62), δ (CCl_4) 1.28 (3 H, t, *J* 7.0 Hz, Me), 1.32 (3 H, s, ring Me), 1.6—2.7 (6 H, m, ring protons), 4.16 (2 H, q, *J* 7.0 Hz, OCH_2), and 4.68 (1 H, m, width 18.1 Hz) (Found: C, 45.6; H, 5.85; Br, 30.1%), M^+ 264/262.

Ethyl 4-*Bromo*-3-*hydroxy*-1-*methyl*-2-*oxocyclohex*-3-*enecarboxylate* (3).—A mixture of the bromide (1a) (2.63 g) and DMSO (20 ml) was stirred at 70 °C for 8 h. The DMSO was then removed *in vacuo*, and the resulting oil was poured into water and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue [a trace of α-diketone (2) was detected by g.l.c. (200 °C; 1.9 kg cm^{-2} He; t_R 3.6 min), but compound (4) (t_R 7.9 min) was not detected] was chromatographed on a silica gel column [benzene–ethyl acetate (10 : 1)] to give the product (1.66 g, 60%). Recrystallization from light petroleum afforded pure (3) as crystals, m.p. and mixed m.p.[4] 80—81 °C (lit.,[4] 80—81 °C).

Ethyl 3-*Bromo*-1-*methyl*-2-*oxocyclohex*-3-*enecarboxylate* (4). —(*a*) A mixture of the bromide (1b) (2.63 g) and DMSO (20 ml) was stirred at 75—78 °C for 20 h. The excess of DMSO was removed *in vacuo* and the resulting oil was poured into water and extracted with ether. The extract was washed with water and dried ($MgSO_4$). G.l.c. analysis (200 °C; 1.9 kg cm^{-2} He) showed the presence of (1b) (t_R 7.5 min), the product (4) (t_R7.9 min), and a small amount of uncharacterized product (t_R 9.6 min). The solvent was removed and the residual oil was chromatographed on a silica gel column (benzene) to give the *bromo-enone* (4) (0.80 g, 30%), b.p. 105—106 °C at 0.6 mmHg, n_D^{20} 1.522 3, $\nu_{max.}$ (neat) 1 723 and 1 698 (C=O), and 1 605 cm^{-1} (C=C); δ (CCl_4) 1.23 (3 H, t, *J* 7.3 Hz, Me), 1.38 (3 H, s, ring Me), 1.6—2.6 (4 H, m, ring protons), 4.11 (2 H, q, *J* 7.3 Hz, OCH_2), and 7.18 (1 H, t, *J* 3.8 Hz, vinylic proton) (Found: C, 46.2; H, 5.1; Br, 29.9. $C_{10}H_{13}BrO_3$ requires C, 46.0; H, 5.0; Br, 30.6%), M^+ 262/260.

(*b*) The dibromide (5)[4] (1.0 g) in DMSO (10 ml) was heated at 75—80 °C for 8 h. Work-up as above afforded the product (4) (0.7 g, 92%), b.p. 105—110 °C at 0.6 mmHg, identical with that derived from (1b).

(*c*) To a stirred solution of ethyl 1-methyl-2-oxocyclohex-3-enecarboxylate (6)[5d] (1.2 g) in DMSO (10 ml) was added bromine (0.53 g) at 30—32 °C over 6 min, and the mixture was stirred at 70—75 °C for 8 h. Work-up as above and distillation of the residual oil (1.1 g) gave the product (4) (0.97 g, 56%), b.p. 100—110 °C at 0.3 mmHg, identical (spectral data) with the other samples.

Ethyl 3-*Bromo*-1-*isopropyl*-2-*oxocyclohexanecarboxylate*

[10] K. S. Schorno, G. H. Adolphen, and E. J. Eisenbraun, *J. Org. Chem.*, 1969, **34**, 2801.

[11] A. Kötz, *Annalen*, 1908, **358**, 183.

(7).—To a stirred solution of ethyl 1-isopropyl-2-oxocyclohexanecarboxylate [12] (6.36 g) in carbon tetrachloride (60 ml) was added bromine (5.28 g) in carbon tetrachloride (4 ml) at room temperature and the mixture was stirred for 2 h. After work-up, distillation of the residual oil provided the bromo derivative (7) (7.86 g, 90%), b.p. 106—108 °C at 0.3 mmHg. This was a mixture of *cis*- and *trans*-isomers (*ca.* 1 : 1 by n.m.r. spectroscopy). The oil was set aside in an ice box; white crystals were precipitated. Filtration and recrystallization from light petroleum ether afforded the solid bromide (7) as *needles*, m.p. 59—60.5 °C, $\nu_{max.}$ (KBr) 1 735 (ester C=O), 1 717 (ketone C=O), 1 213, 1 194, and 1 023 cm^{-1}; δ (CCl_4) 0.88 (3 H, d, *J* 7.0 Hz), 0.97 (3 H, d, *J* 7.0 Hz), 1.23 (3 H, t, *J* 7.0 Hz), 1.6—2.7 (7 H, m, ring protons), 4.27 (2 H, q, *J* 7.0 Hz), and 4.71 (1 H, m, width 18 Hz) (Found: C, 49.35; H, 6.45; Br, 27.6. $C_{12}H_{19}BrO_3$ requires C, 49.5; H, 6.6; Br, 27.5%).

Ethyl 3,3-*Dibromo*-1-*isopropyl*-2-*oxocyclohexanecarboxylate* (9).—Ethyl 1-isopropyl-2-oxocyclohexanecarboxylate (4.24 g) in carbon tetrachloride (50 ml) and bromine (7.0 g) gave the *dibromide* (9) (6.9 g, 93%) as needles, m.p. 66—67 °C (from light petroleum), $\nu_{max.}$ (KBr) 1 735 (ester C=O) and 1 716 cm^{-1} (ketone C=O); δ (CCl_4) 0.76 (3 H, d, *J* 7.0 Hz), 0.85 (3 H, d, *J* 7.0 Hz), 1.26 (3 H, t, *J* 7.0 Hz), 1.6—3.0 (7 H, m), and 4.14 and 4.16 (2 H, q, *J* 7.0 Hz) (Found: C, 38.8; H, 5.15; Br, 42.7. $C_{12}H_{18}Br_2O_3$ requires C, 38.9; H, 4.9; Br, 43.2%).

Ethyl 3-*Bromo*-1-*isopropyl*-2-*oxocyclohex*-3-*enecarboxylate* (8).—(*a*) A mixture of compound (7) (0.63 g) and DMSO (9 ml) was warmed at 130—150 °C for 5 h. Then the excess of DMSO was removed and the resulting oil was poured into water and extracted with ether. After work-up, the residual oil was chromatographed on a silica gel column (benzene) to give pure *product* (8) (0.12 g, 20%), b.p. 100—105 °C at 0.3 mmHg, $\nu_{max.}$ (neat) 3 030 (=CH), 1 730, 1 698 (C=O of ester and ketone), and 1 610 cm^{-1} (C=C); δ (CCl_4) 0.87 (3 H, d, *J* 7.0 Hz), 0.91 (3 H, d, *J* 7.0 Hz), 1.22 (3 H, t, *J* 7.0 Hz), 1.6—2.7 (5 H, m), 4.10 (2 H, q, *J* 7.0 Hz), and 7.10 (1 H, t, *J* 4.0 Hz, vinylic proton) (Found: C, 50.5; H, 6.1. $C_{12}H_{17}BrO_3$ requires C, 49.9; H, 5.9%), M^+ 290/288.

(*b*) The dibromide (9) (1.0 g) in DMSO (10 ml) was heated at 100 °C for 5 h. Work-up afforded the product (8) (0.47 g, 60%) as an oil, b.p. 100—102 °C at 0.3 mmHg, identical with that derived from (7).

Diethyl 3-*Bromo*-2-*oxocyclohexane*-1,1-*dicarboxylate* (10).—To a stirred solution of diethyl 2-oxocyclohexane-1,1-dicarboxylate [13] (4.84 g) in carbon tetrachloride (45 ml), bromine (3.52 g) in carbon tetrachloride (5 ml) was added dropwise at 3—5 °C over 1 h, and the mixture was stirred for 2 h at room temperature. Work-up as for (1a) provided the pure *product* (10) (5.3 g, 83%), b.p. 130 °C at 0.35 mmHg, $\nu_{max.}$ (neat) 1 748, 1 730, and 1 720 cm^{-1} (C=O of ester and ketone); δ (CCl_4) 1.31 (6 H, t, *J* 7.2 Hz, Me), 1.5—3.0 (6 H, m, ring protons), 4.27 (2 H, q, *J* 7.2 Hz, OCH_2), 4.30 (2 H, q, *J* 7.2 Hz, OCH_2), and 4.95 (1 H, m, width 18.1 Hz) (Found: C, 44.65; H, 5.2; Br, 24.9. $C_{12}H_{17}BrO_5$ requires C, 44.9; H, 5.3; Br, 24.9%).

Diethyl 3,3-*Dibromo*-2-*oxocyclohexane*-1,1-*dicarboxylate* (12).—To a stirred solution of diethyl 2-oxocyclohexane-1,1-dicarboxylate (2.42 g) in carbon tetrachloride (18 ml), bromine (3.52 g) in carbon tetrachloride (2 ml) was added at room temperature and the mixture was then stirred for 2 h at 45 °C. Work-up in the usual way and distillation (b.p. 153—155 °C at 0.5 mmHg) provided the *product* (12) (2.8 g, 70%), which solidified spontaneously; m.p. 51.5—52.5 °C (from light petroleum), $\nu_{max.}$ (KBr) 1 762, 1 730, and 1 720 cm^{-1} (C=O); δ (CCl_4) 1.31 (6 H, t, *J* 7.2 Hz, Me), 1.5—3.1 (6 H, m, ring protons), and 4.28 (4 H, q, *J* 7.2 Hz) (Found: C, 35.85; H, 4.1; Br, 39.9. $C_{12}H_{16}Br_2O_5$ requires C, 36.0; H, 4.0; Br, 40.0%).

Diethyl 3-*Bromo*-2-*oxocyclohex*-3-*ene*-1,1-*dicarboxylate* (11).—(*a*) A mixture of compound (10) (2.21 g) and DMSO (17.3 ml) was stirred at 73—77 °C for 7 h and then for 8 h at 80—85 °C. The DMSO was removed, and the resulting oil was poured into water and extracted with ether. After the usual work-up, the orange residual oil was distilled to give the *product* (11) (1.40 g, 63.8%), b.p. 120—125 °C at 0.25 mmHg, $\nu_{max.}$ (neat) 1 730, 1 720, and 1 695 (C=O), and 1 603 cm^{-1} (C=C); δ (CCl_4) 1.30 (6 H, t, *J* 7.2 Hz, Me), 2.1—2.7 (4 H, m, ring protons), 4.24 (4 H, q, *J* 7.2 Hz, OCH_2), and 7.25 (1 H, t, *J* 4.1 Hz, vinylic proton) (Found: C, 44.85; H, 4.75; Br, 25.2. $C_{12}H_{15}BrO_5$ requires C, 45.15; H, 4.75; Br, 25.0%), M^+ 320/318.

(*b*) The dibromide (12) (1.0 g) in DMSO (10 ml) was heated at 75—80 °C for 8 h. Work-up as above yielded the *product* (11) (0.65 g, 81.6%), b.p. 110—120 °C at 0.2 mmHg, identical with that derived from (10).

Diethyl 3-*Bromo*-2-*oxocyclopentane*-1,1-*dicarboxylate* (13).—To a stirred solution of diethyl 2-oxocyclopentane-1,1-dicarboxylate [13] (6.72 g) in carbon tetrachloride (30 ml), bromine (5.28 g) in carbon tetrachloride (10 ml) was added at room temperature and the mixture was stirred for 2 h. After work-up, distillation of the residual oil provided the product (13) (7.5 g, 81%), b.p. 125—126 °C at 0.25 mmHg, n_D^{25} 1.482 0, $\nu_{max.}$ (neat) 1 768, 1 730, and 1 720 cm^{-1} (C=O); δ (CCl_4) 1.30 (3 H, t, *J* 7.2 Hz, Me), 1.32 (3 H, t, *J* 7.2 Hz, Me), 2.0—3.0 (4 H, m, ring protons), 4.24 (2 H, q, *J* 7.2 Hz, OCH_2), 4.28 (2 H, q, *J* 7.2 Hz, OCH_2), and *ca.* 4.3 (1 H, m) (Found: C, 42.9; H, 5.1. $C_{11}H_{15}BrO_5$ requires C, 43.0; H, 4.9%).

Diethyl 3-*Bromo*-2-*oxocyclopent*-3-*ene*-1,1-*dicarboxylate* (14).—A solution of compound (13) (3.07 g) in DMSO (25 ml) was warmed at 70 °C for 8 h. After work-up, the residual oil was distilled to give the *product* (14) (1.90 g, 62%), b.p. 124 °C at 0.25 mmHg, $\nu_{max.}$ (neat) 1 748, 1 730, and 1 720 cm^{-1} (C=O), δ (CCl_4) 1.31 (6 H, t, *J* 7.2 Hz, Me), 3.28 (2 H, d, *J* 3.0 Hz, ring protons), 4.26 (4 H, q, *J* 7.2 Hz, OCH_2), and 7.83 (1 H, t, *J* 3.0 Hz, vinylic proton) (Found: C, 43.35; H, 4.6. $C_{11}H_{13}BrO_5$ requires C, 43.3; H, 4.3%), M^+ 306/304.

Diethyl 6-*Methyl*-4-*oxotetrahydropyran*-3,3-*dicarboxylate* (15).—To a stirred mixture of formalin (8.92 g), potassium carbonate (0.26 g), and water (1 ml) diethyl 2-oxopent-3-ene-1,1-dicarboxylate [14] (15.5 g) was added dropwise at −5 °C over 30 min. The mixture was stirred for 3 h at room temperature. Extraction with ether and work-up in the usual way afforded an oil (16.4 g), $\nu_{max.}$ (neat) 3 500 cm^{-1} (OH). A mixture of this crude oil and 15% sulphuric acid (95 ml) was stirred at 65—70 °C for 11 h, then extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. Distillation gave the *product* (15) (7.4 g, 40%), b.p. 108—111 °C at 0.3 mmHg, n_D^{20} 1.453 3, $\nu_{max.}$ (neat) 1 755 and 1 732 (C=O), and 1 260, 1 235, 1 090, and 1 070 cm^{-1} (C–O–C), δ (CCl_4) 1.28 (3 H, d, *J* 6.8 Hz,

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ring Me), 1.30 (3 H, t, *J* 7.2 Hz), 1.34 (3 H, t, *J* 7.2 Hz), 2.48 (1 H, d, *J* 4.5 Hz, H-5e), 2.52 (1 H, d, *J* 9.0 Hz, H-5a), 3.6—3.9 (1 H, m, H-6a), 3.97 (1 H, d, *J* 12 Hz, H-2a), 4.25 (2 H, q, *J* 7.2 Hz), 4.30 (2 H, q, *J* 7.2 Hz), and 4.59 (1 H, d, *J* 12 Hz, H-2e) (Found: C, 55.9; H, 7.3. $C_{12}H_{18}O_6$ requires C, 55.8; H, 7.05%).

Diethyl 5-Bromo-6-methyl-4-oxotetrahydropyran-3,3-dicarboxylate (16).—To a solution of compound (15) (10.3 g, 0.04 mol) in carbon tetrachloride (60 ml), bromine (12.8 g, 0.08 mol) in carbon tetrachloride (20 ml) was added at 47—50 °C, and the mixture was stirred for 7 h under reflux. The excess of bromine was destroyed with sodium hydrogen carbonate and sodium disulphite. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. The residual oil was distilled to afford the *product* (16) (11.9 g, 88.6%), b.p. 132—133 °C at 0.3 mmHg, $\nu_{max.}$ (neat) 1 755 and 1 732 (C=O), and 1 260 and 1 235 cm^{-1} (C–O–C); δ (CCl_4) 1.36 (3 H, t, *J* 7.2 Hz), 1.38 (3 H, t, *J* 7.2 Hz), 1.54 (3 H, d, *J* 8.1 Hz, ring Me), 3.6—3.9 (1 H, m, H-6a), 4.07 (1 H, d, *J* 11.8 Hz, H-2a), 4.35 (2 H, q, *J* 7.2 Hz), 4.40 (2 H, q, *J* 7.2 Hz), 4.70 (1 H, d, *J* 11.8 Hz, H-2e), 4.71 (1 H, d, *J* 10.3 Hz, H-5a) (Found: C, 43.2; H, 5.2. $C_{12}H_{17}BrO_6$ requires C, 42.75; H, 5.1%).

Diethyl 3-Bromo-3,4-dihydro-2-methyl-4-oxo-2H-pyran-3,3-dicarboxylate (17).—A solution of *compound* (16) (3.37 g) in DMSO (30 ml) was stirred at 100—130 °C for 13 h. After work-up, the residual oil was chromatographed on a silica gel column [benzene–ethyl acetate (30 : 1)] to give pure *product* (17) (1.0 g, 30%), b.p. 117—120 °C at 0.1 mmHg, $\nu_{max.}$ (neat) 1 745 (ester C=O), 1 690 (ketone C=O), and 1 590 cm^{-1} (C=C), δ (CCl_4) 1.31 (6 H, t, *J* 7.2 Hz), 2.26 (3 H, s), 4.29 (4 H, q, *J* 7.2 Hz), and 4.80 (2 H, s) (Found: C, 43.7; H, 4.7. $C_{12}H_{15}BrO_6$ requires C, 43.0; H, 4.5%), M^+ 336/334.

Oxidation of Ethyl 1,3-Dibromo-2-oxocyclohexanecarboxylate (18).—A solution of the ester (18) [10] (3.28 g) in DMSO (20 ml) was warmed at 70—75 °C for 7 h. Then the DMSO was removed *in vacuo* and the resulting oil was diluted with chloroform (30 ml). The solution was washed with water, dried ($MgSO_4$), and concentrated, and the residual oil (2.9 g) was chromatographed on a silica gel column (benzene). An early fraction afforded ethyl 3,5-dibromosalicylate (20) (0.50 g, 15.4%) as needles, m.p. 100—101 °C (lit.,[15] 100—101 °C), $\nu_{max.}$ (KBr) 3 070 (OH), 1 672 (C=O), and 1 601 cm^{-1} (C=C); δ (CCl_4) 1.45 (3 H, t, *J* 7.0 Hz), 4.41 (2 H, q, *J* 7.0 Hz), 7.78 (2 H, m), and 11.22 (1 H, s), M^+ 326/324/322. A later fraction provided ethyl 5-bromosalicylate (19) (1.60 g, 65.3%) as a liquid, b.p. 95—100 °C at 0.1 mmHg, which solidified spontaneously; m.p. 49—50 °C (lit.,[15] 49—50 °C), $\nu_{max.}$ (KBr) 3 080 (OH), 1 670 (C=O), and 1 602 cm^{-1} (C=C); δ (CCl_4) 1.43 (3 H, t, *J* 7.0 Hz), 4.38 (2 H, q, *J* 7.0 Hz), 6.64 (1 H, m), 7.62 (2 H, m), and 11.22 (1 H, s), M^+ 246/244.

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