Chemistry of α-Halo Aldehydes. IV. Reaction of 2-Halo-2-methylpropanal with Acylacetates in the Presence of Base[1]

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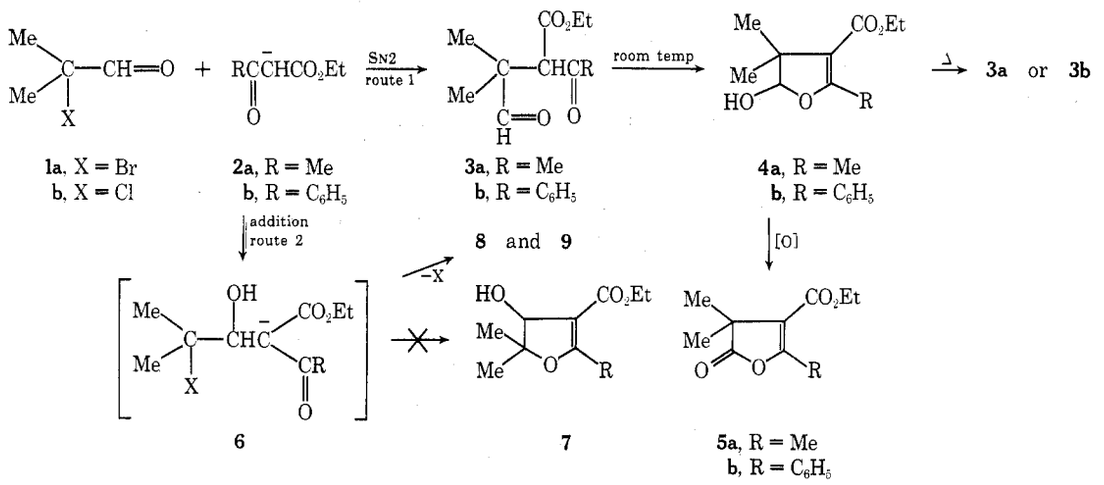
The reaction of 2-halo-2-methylpropanal (**1**) with acylacetate (**2**) in basic media has been investigated. In nonaqueous media, tautomeric mixtures of 4-substituted 2,2-dimethyl-3-ethoxycarbonyl-4-oxobutanal (**3**) and 5-substituted ethyl 2-hydroxy-3,3-dimethyl-2,3-dihydrofuran-4-carboxylate (**4**) were obtained. When kept for 2 weeks at room temperature, this mixture equilibrated to give mainly **4**. The cyclic hemiacetal **4** can be reconverted partly to **3** by heating. The chromic acid oxidation of **4** gave γ-substituted α,α-dimethyl-β-ethoxycarbonyl-$\Delta^{\beta,\gamma}$-butenolide (**5**). In aqueous media, the enolate anion of **2** attacked the carbonyl carbon of **1** to give α-acyl-β-acylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (**9**). Compound **9** was decomposed to **2** and α-acyl-γ,γ-dimethyl-$\Delta^{\alpha,\beta}$-butenolide (**8**) when heated at 160–170° under reduced pressure. The butenolide **8** readily reacted with 1 mol of acylacetate in aqueous K_2CO_3 to regenerate the saturated butyrolactone **9**. While the alkaline hydrolysis of α-acetyl-β-acetylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (**9a**) underwent both deacylation in the side chain and deacylation at the α position of the lactone ring to give terpenylic acid (**11**), that of α-benzoyl-β-benzoylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (**9b**) afforded β-phenacyl-γ,γ-dimethyl-γ-butyrolactone (**10**) as a result of decaylation only at the α position of the lactone ring.

We have been studying the reactions of α-halo aldehyde with active hydrogen compounds.[2-4] In the previous paper,[4] we reported the reaction of 2-halo-2-methylpropanal (**1**) with malonic ester, which gave γ-butyrolactones of versatile utility such as terpenylic acid. Franke, *et al.*,[5] in 1922 reported that the base-catalyzed condensation of 2-bromo-2-methylpropanal (**1a**) with ethyl acetoacetate (**2a**) afforded a product with the formula of $C_{10}H_{16}O_4$ and undetermined structure. It was anticipated that 3-hydroxydihydrofuran (**7**) might be produced which would be promising as the precursor to make 3-furanones such as bullatenone;[6] hence we became interested in investigating the reaction of **1** with benzoylacetoacetate (**2b**) as well as with **2a**. Because of the bifunctionality of the substrate **1**, two pathways can be postulated for the reaction as is shown in Scheme I. One involves SN2 substitution leading to 1,4-dioxo compound **3**, which may be cyclized to 2-hydroxydihydrofuran **4** (route 1). Another possibility is nucleophilic attack of the enolate anion of **2** on the carbonyl carbon of the substrate **1** (route 2). As the nature of the solvent appreciably influences the pathway,[4] we conducted the reaction under various conditions in order to study the solvent effect: (a) using sodium ethoxide as base and absolute ethanol as solvent (same condition as Franke's);[5] (b) using sodium ethoxide in dry ether; (c) using potassium carbonate in tetrahydrofuran (THF); (d) using potassium carbonate in water. The present paper describes and discusses the results of these reactions.

Results and Discussion

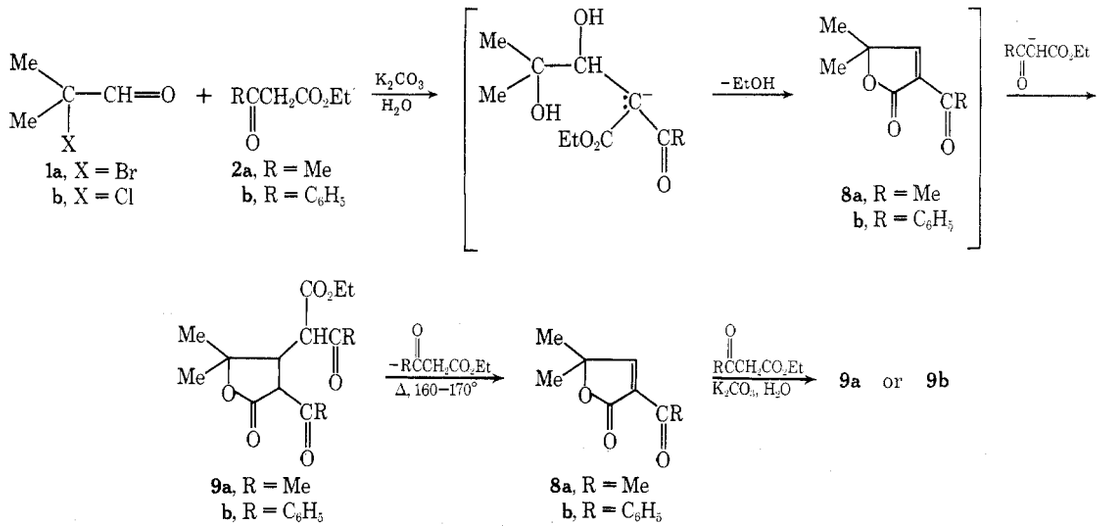
In all cases except d, tautomeric mixtures of **3** and **4** were obtained. Structural assignments of the products were made principally on the basis of ir and nmr spectra. Compound **3** seems to predominate in the mixture during the distillation; however, these compounds gradually equilibrate *via* an intramolecular conversion. For instance, from the reaction of 2-bromo-2-methylpropanal (**1a**) with **2a** under the condition b, a tautomeric mixture[7] of 2,2-dimethyl-3-ethoxycarbonyl-4-oxopentanal (**3a**) and ethyl 2-hydroxy-3,3,5-trimethyl-2,3-dihydrofuran-4-carboxylate (**4a**) was obtained as an oily product in a 67% yield.[8] The elemental analysis and mass spectrum of this oil were compatible with the formula $C_{10}H_{16}O_4$ reported by Franke, *et al.*[5] The nmr spectrum of freshly distilled product exhibited proton signals of **3a** at δ 2.24 (s, $COCH_3$), 3.83 (s, $CHCO_2C_2H_5$), and 9.62 ppm (s, CHO), while **4a** showed three singlets at 2.19 (=CCH_3), 2.98 (OH), and 5.29 ppm (methine proton), respectively. When kept for 2 weeks at room temperature, this mixture equili-

Scheme I



1a, X = Br; **b**, X = Cl
2a, R = Me; **b**, R = C_6H_5
3a, R = Me; **b**, R = C_6H_5
4a, R = Me; **b**, R = C_6H_5
6
7
5a, R = Me; **b**, R = C_6H_5

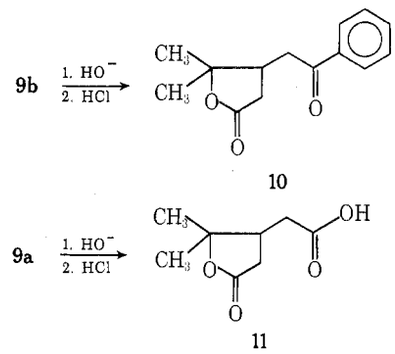
Scheme II



brated to give a ratio of **4a** to **3a** of *ca.* 40:1. The ir bands at 1670 and 1635 cm^{-1} appear in the spectrum as the absorption at 1720 cm^{-1} disappears, indicating that transformation of the system to an α,β-unsaturated ester has occurred. The cyclic hemiacetal **4a** can be reconverted partly to **3a** by heating. Ethyl benzoylacetate (**2b**) reacted with **1b** similarly, affording ethyl 2,2-dimethyl-3-ethoxycarbonyl-4-phenyl-4-oxobutanal (**3b**) which, when kept at room temperature for several days, tautomerized to ethyl 2-hydroxy-3,3-dimethyl-5-phenyl-2,3-dihydrofuran-4-carboxylate (**4b**).

The oxidation of **4a** with CrO_3 gave α,α,γ-trimethyl-β-ethoxycarbonyl-$\Delta^{\beta,\gamma}$-butenolide (**5a**) in a 64% yield. The ir spectrum of **5a** showed a strong band at 1800 cm^{-1} due to $\Delta^{\beta,\gamma}$-butenolide carbonyl.[9] Chromic acid oxidation of **4b** also gave $\Delta^{\beta,\gamma}$-butenolide (**5b**) in a 40% yield.

In contrast with reactions under nonaqueous conditions, the enolate anion of acylacetate (**2**) attacked the carbonyl group of **1** in aqueous media to give α-acyl-β-acylethoxycarbonylmethyl-γ-butyrolactone (**9**). The reaction of **1b** with acetoacetate in aqueous K_2CO_3 afforded α-acetyl-β-acetylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (**9a**) in a 91% yield. From the reaction of **1b** with **2b** in aqueous K_2CO_3, α-benzoyl-β-benzoylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (**9b**) was obtained as a crystalline product in a 94% yield. The butyrolactone **9** eliminated 1 mol of ethyl acylacetate to give α-acyl-γ,γ-dimethyl-$\Delta^{\alpha,\beta}$-butenolide (**8**) when heated at 160–170° under reduced pressure. Mass spectra of both **8b** and **9b** showed a clean molecular ion peak of **8b** at m/e 216.[10] Furthermore, the butenolide **8** readily reacted with 1 mol of acylacetate in aqueous K_2CO_3 solution to regenerate the saturated butyrolactone **9** in good yields. Based on this fact, it is reasonable to consider that the butenolide **8** is produced first in the reaction of **1** and **2**, and then undergoes Michael addition of **2** as is shown in Scheme II. In aqueous alkaline solution, 2-halo-2-methylpropanal promptly undergoes displacement of halogen to give 2-hydroxy-2-methylpropanal (**1c**).[11] Therefore, it is possible that the hydroxy aldehyde **1c** produced in the reaction medium is the real substrate in this reaction.[12] Compound **9b** can be prepared also by the condensation of **1c** with enolate anion of **2b** even in nonaqueous media. The alkaline hydrolysis of the lactonic ester **9b** is complicated by the deacylation at the α position affording β-phenacyl-γ,γ-dimethyl-γ-butyrolactone (**10**). The lactonic ester **9a** underwent both deacylation in the side chain and deacylation at the α position of the lactone ring under the same condition as above, giving *dl*-terpenylic acid (**11**) in a 52



% yield. The reaction described in the present article will be helpful for synthesizing ketone carrying γ-butyrolactone or $\Delta^{\alpha,\beta}$-butenolide rings.

Experimental Section

Melting points and boiling points are uncorrected. Elemental analyses were carried out by Mr. Eiichiro Amano. We are indebted to Mr. Heizan Kawamoto and Miss Hiromi Ootani for nmr measurements. Analytical determinations by glpc were performed on a Hitachi Model K-53 gas chromatograph filled with the following materials (3 mm o.d. × 1 m): A, 10% Apiezone Grease L on Chromosorb W; B, 10% polyneopentyl glycol succinate on Chromosorb W. The preparative isolations by glpc were performed on a Yanagimoto Model GCG-550T gas chromatograph (3 mm o.d. × 2.25 m, 10% Apiezone Grease L on Chromosorb W). The nuclear magnetic resonance spectra (60 MHz) were recorded with Hitachi Model R-24 and R-20 spectrometers. Mass spectra were obtained with a Hitachi Model RMS-4 mass spectrometer. Thin layer chromatography (tlc) was done on silica gel GF_{254} (E. Merck AG, Darmstadt) with layers of 0.25-mm thickness. Preparative tlc was performed on silica gel PF_{254} (E. Merck AG, Darmstadt) with 1.0-mm layers.

Starting materials such as 2-bromo-2-methylpropanal (**1a**),[13] 2-chloro-2-methylpropanal (**1b**),[14] 2-hydroxy-2-methylpropanal (**1c**),[15] and ethyl benzoylacetate (**2b**)[16] were prepared by procedures described in the literature.

Tautomeric Mixture of 2,2-Dimethyl-3-ethoxycarbonyl-4-oxopentanal (3a) and Ethyl 2-Hydroxy-3,3,5-trimethyl-2,3-dihydrofuran-4-carboxylate (4a). Procedure A (Condition a). An ethanolic solution of ethyl sodioacetoacetate was prepared by dissolving 1.9 g (0.082 mol) of sodium in the mixture of 10.7 g (0.082 mol) of ethyl acetoacetate (**2a**) and 50 ml of ethanol. To the stirred solution, 12.3 g (0.082 mol) of **1a** was added dropwise at 0°. The mixture was stirred for 30 min at 0° and then for 1 hr at room temperature. After being refluxed for an additional 1 hr,

the mixture was poured into a large excess of water. The organic layer was extracted with ether and dried over $MgSO_4$. After removal of the solvent, the residual oil was distilled to give 4.3 g (26%) of a tautomeric mixture[17] of **3a** and **4a** (1:4):[7] bp 102–103° (3 mm); ir (neat)[18] 3400 (OH), 1720 (C=O), 1690 (C=O), 1635 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.24 (s, 7.5, CH_3), 1.28 (t, 3.75, J = 7 Hz, $CO_2CH_2CH_3$), 2.19 (s, 3, $=CCH_3$), 2.24 (s, 0.75, $COCH_3$), 2.98 (broad s, 1, OH), 3.83 (s, 0.25, $CHCO_2Et$), 4.19 (q, 2, J = 7 Hz, ester $-CH_2-$ of **4a**), 4.24 (q, 0.55, J = 7 Hz, ester $-CH_2-$ of **3a**), 5.29 [s, 1, $-OCH(OH)-$], 9.62 (s, 0.25, CHO); mass spectrum (70 eV) m/e (rel intensity) 200 (37, M^+), 185 (25, $M^+ - CH_3$), 171 (49, $M^+ - C_2H_5$), 157 (30, $M^+ - COCH_3$), 155 (38), 139 (49, $M^+ - COCH_3 - H_2O$), 129 (96, $CH_3COCHCO_2Et^+$), 125 (100), 113 (75), 111 (63).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.21; H, 7.78.

The ir and nmr spectra of this product changed slowly until the spectral shift data ceased to be observable 2 weeks after distillation: ir[19] (neat) 3400 (OH), 1690, 1670 (C=O), 1635 cm^{-1} (C=C); nmr ($CDCl_3$) δ 1.24 (s, 6, 2 CH_3), 2.16 (s, 3, $=CCH_3$), 4.10 (broad s, 1, OH), 4.18 (q, 2, J = 7 Hz, ester $-CH_2-$ of **4a**), 5.29 [s, 1, $-OCH(OH)$], and 9.62 (s, trace, CHO).

Procedure B (Condition b). Sodium (2.3 g, 0.1 mol) was dissolved in 15 ml of absolute ethanol with cooling. After complete evaporation of excess ethanol, 13.0 g (0.1 mol) of **2a** dissolved in 30 ml of dry ether was added. To the resulting mixture, 15.1 g (0.1 mol) of **1a** was added dropwise at 0° in the course of 1 hr. The stirring was continued for 2 hr at 0°, and then for an additional 2-hr period at room temperature. After being allowed to stand overnight, the mixture was worked up in the same way as in procedure A to give 13.3 g (67%) of the tautomeric mixture of **3a** and **4a** (7:13),[7] bp 116–119° (6 mm). Glpc analysis[20] showed one peak with a retention time of 13 min. Both ir and nmr spectra showed patterns similar to those of the product described in the preceding section. In 2 weeks after distillation, the ratio of **4a** to **3a** in the mixture changed to 40:1.[7]

Procedure C (Condition c). To a dry THF solution (50 ml) of potassium carbonate (16.8 g, 0.12 mol) and **2a** (15.6 g, 0.12 mol), 12.8 g (0.12 mol) of **1b** was added dropwise at 0° with stirring. The mixture was stirred for 40 hr at room temperature and for an additional 10-hr period at 50°. It was worked up as described above to give 10.5 g (44%) of a mixture of **3a** and **4a**, bp 130–134° (15 mm). Its ir and nmr spectra were almost identical with those of the product in procedure B, finally exhibiting only the characteristic pattern of **4a**.[19]

Ethyl 2,2-Dimethyl-3-ethoxycarbonyl-4-phenyl-4-oxobutanal (3b) and Ethyl 2-Hydroxy-3,3-dimethyl-5-phenyl-2,3-dihydrofuran-4-carboxylate (4b). Procedure A. To a suspension of 17.4 g (0.125 mol) of potassium carbonate in 50 ml of dry THF was added 24 g (0.125 mol) of **2b** at room temperature. After the mixture was stirred for 20 min, 13.3 g (0.125 mol) of **1b** was added dropwise at 0°. The stirring was continued for 4 hr at room temperature, and then for an additional 11 hr at 65°. The reaction mixture was filtered to remove solid material, which, after being dissolved in water, was extracted with ether. The filtrate combined with the ethereal extract was washed with water and then dried over $MgSO_4$. It was subjected to vacuum distillation to give 20.8 g of **3b**, clean oil, yield 63%: bp 156–157° (0.06 mm); ir (neat)[18] 2720 (CHO), 1725 (C=O), 1683 (C=O), 1595 and 1577 cm^{-1} (benzene C=C); nmr ($CDCl_3$) δ 1.13 (t, 3, J = 7 Hz, $CO_2CH_2CH_3$), 1.22 (s, 3, CH_3), 1.24 (s, 3, CH_3), 4.11 (q, 2, J = 7 Hz, $CO_2CH_2CH_3$), 4.65 (s, 1, $-CHCO_2Et$), 7.22–8.1 (m, 5, C_6H_5), 9.79 (s, 1, -CHO); mass spectrum (70 eV) m/e (rel intensity) 262 (3, M^+), 234 (31, $M^- - CH_2{=}CH_2$), 192 (19, $PhCOCH_2CO_2Et$), 187 (30, $M^+ - CO_2Et$), 173 (22), 161 (79), 129 (93), 105 (100, PhCO), 101 (74).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.66; H, 7.12.

The patterns of ir and nmr spectra of **3b** shifted completely to those of **4b** in 2 weeks after distillation. **3b** was quantitatively transformed to white crystals of **4b**: mp 78–79° after recrystallization from benzene–petroleum ether; ir (KBr) 3430 (OH), 1678 (conjugated C=O), 1620 (C=C), 1600 and 1573 cm^{-1} (benzene C=C); nmr ($CDCl_3$) δ 1.13 (t, 3, J = 7 Hz, $CO_2CH_2CH_3$), 1.32 (s, 6, 2 CH_3), 4.0 (broad s, 1, OH), 4.08 (q, 2, J = 7 Hz, $CO_2CH_2CH_3$), 5.36 (d,[21] 1, J = 6 Hz, $-OCHOH-$), 7.2–7.7 (m, 5, C_6H_5); mass spectrum (70 eV) m/e (rel intensity) 262 (9, M^+), 247 (2, $M^+ - CH_3$), 234 (28, $M^+ - CH_2{=}CH_2$), 192 (21, $PhCOCH_2CO_2Et$), 187 (49, $M^+ - CO_2Et$), 173 (25), 161 (88), 129 (99), 105 (100, PhCO), 101 (75).

Distillation of 4b under diminished pressure regenerated **3b** quantitatively, bp 130° (0.1 mm).

Procedure B. To the mixed solution of ethyl sodiobenzoylacetate (0.05 mol) in 140 ml of ether was added dropwise 5.4 g (0.05 mol) of **1b** at 5–10° with stirring. The mixture was stirred for 5 hr at 30°, and then was made acidic with dilute HCl. From the ethereal extract, which was worked up in the usual way, 3.5 g of **3b** was collected by distillation, yield 27%, bp 140–143° (0.06 mm). This product also tautomerized quantitatively to the crystalline product of **4b**.

Procedure C. To a solution of **2b** (1.92 g, 0.01 mol) and **1b** (1.07 g, 0.01 mol) in 10 ml of dry hexamethylphosphoramide was added 1.38 g (0.01 mol) of potassium carbonate with moderate coolling. The mixture, stirred for 23 hr at room temperature, was poured into a large excess of water and then acidified with 10% HCl. The ethereal extract of the organic layer was washed with water and dried over $MgSO_4$. After removal of the solvent, the residual oil was distilled to give 1.15 g (44%) of **3b**, bp 141–143° (0.05 mm).[22]

α,α,γ-Trimethyl-β-ethoxycarbonyl-$\Delta^{\beta,\gamma}$-butenolide (5a). To a mixed solution of 8 g (0.08 mol) of chromium trioxide in 20 ml of 70% acetic acid was added 8.0 g (0.04 mol) of the tautomeric mixture of **3a** and **4a** (7:13)[7] in several portions with cooling. The mixture was stirred for 2 hr at room temperature and then for 2 hr at 60°. After 80 ml of water was added to the mixture, it was extracted with ether. The extract was washed with water and dried over Na_2SO_4. Removal of the solvent left 6.8 g of a clean oil[23] which showed two peaks on glpc analysis.[24] The components, retention times (minutes), and integrated percentages are as follows: 1, 0.8, 15%; 2, 5.2, 74%. The retention time of component 1 was identical with that of acetic acid. Component 2 was collected by preparative glpc and identified as **5a**: yield 64%; nmr ($CDCl_3$) δ 1.30 (t, 3, J = 7 Hz, $CO_2CH_2CH_3$), 1.41 (s, 6, 2 CH_3), 2.40 (s, 3, $=CCH_3$), 4.22 (q, 2, J = 7 Hz, $CO_2CH_2CH_3$); mass spectrum (70 eV) m/e (rel intensity) 198 (38, M^+), 183 (20, $M^+ - CH_3$), 170 (7, $M^+ - CH_2{=}CH_2$), 159 (14), 155 (28, $M^+ - CH_3CO$), 153 (18), 125 (69, $M^+ - CO_2Et$), 124 (39), 109 (38), 96 (100).

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.39; H, 7.12. Found: C, 60.68; H, 7.00.

α,α-Dimethyl-β-ethoxycarbonyl-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (5b). Compound **4b** (1.7 g, 0.0065 mol) was oxidized with chromium trioxide (5 g, 0.05 mol) in 77% acetic acid (13 ml) in the same way as **4a**. From the reaction mixture, 0.8 g of a clean oil was obtained. Glpc analysis[25] of this oil showed two peaks. The components, retention times, and integrated percentages are as follows: 1, 24.8, 85%; 2, 40, 15%. The retention time of component 2 was identical with that of **4b**. Component 1 was collected by preparative glpc and identified as **5b**: yield 40%; ir (neat) 1806 (lactone C=O), 1723 and 1700 (ester C=O), 1632 (C=C), 1596 and 1578 cm^{-1} (benzene C=C); nmr ($CDCl_3$) δ 1.22 (t, 3, J = 7 Hz, $CO_2CH_2CH_3$), 1.56 (s, 6, 2 CH_3), 4.20 (q, 2, J = 7 Hz, $CO_2CH_2CH_3$), 7.3–8.1 (m, 5, C_6H_5); mass spectrum (70 eV) m/e (rel intensity) 260 (29, M^+), 245 (44, $M^+ - CH_3$), 231 (3), 199 (25), 187 (18, $M^+ - CO_2Et$), 171 (6), 158 (45), 105 (100, PhCO), 77 (75, C_6H_5).

Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 69.25; H, 6.15.

α-Acetyl-β-acetylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (9a). To a solution of **1b** (6.4 g, 0.06 mol) in 50 ml of water was added 8.4 g (0.06 mol) of potassium carbonate in several portions. After the mixture was stirred for 2 hr at room temperature, 7.8 g (0.06 mol) of **2a** was added. After being stirred for 14 hr at room temperature, it was neutralized with dilute HCl. The organic layer was extracted with ether and the extract was dried over $MgSO_4$. After removal of the solvent, 7.7 g of crude **9a** was obtained: yield 91%;[26] mp 168–169° dec after one recrystallization from the mixed solvent of acetone–*n*-hexane (1:1, v/v); ir (Nujol) 3400 (enolic OH), 1740 and 1710 cm^{-1} (C=O); nmr[27] (CD_3SOCD_3) δ 1.20 (t, 3, J = 7.5 Hz, $CO_2CH_2CH_3$), 1.30 (s, 6, 2 CH_3), 1.49 (s, 2.9), 2.13 (s, 0.2), 2.48 (d, J = 12 Hz), 2.90 (d, 0.8, J = 9 Hz), 3.18 (s, 1.4), 3.31 (s, 1.6), 3.62 (d, 0.6, J = 2 Hz), 3.80 (d, 0.4, J = 2 Hz), 4.15 (q, 2, J = 7.5 Hz, $CO_2CH_2CH_3$), 5.29 (s, 0.8); mass spectrum (70 eV) m/e (rel intensity) 284 (0.5, M^+), 266 (9, $M^+ - H_2O$), 194 (27), 180 (44), 136 (94), 134 (100), 108 (91), 107 (95), 80 (72), 79 (75).

Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.63; H, 6.70.

α-Acetyl-γ,γ-dimethyl-$\Delta^{\alpha,\beta}$-butenolide (8a). Procedure A. To a solution of **2a** (6.5 g, 0.05 mol) and potassium carbonate (3.5 g, 0.025 mol) in water (50 ml) was added 7.6 g (0.05 mol) of **1a** at

room temperature with stirring. The mixture was stirred at room temperature for 24 hr, and finally at 50° for 20 hr. After being neutralized with dilute HCl, it was extracted with ether. The extract was washed with water and dried over Na_2SO_4. Removal of the solvent left 7.1 g of yellow oil which, on distillation, gave 4.8 g (62%) of **8a**: bp 93–102° (5 mm); mp 64–65° (benzene); ir (Nujol) 1750 (conjugated lactone C=O), 1670 (acetyl C=O), 1620 cm^{-1} (conjugated C=C); nmr ($CDCl_3$) δ 1.58 (s, 6, 2 CH_3), 2.55 (s, 3, $COCH_3$), 8.10 (s, 1, =CH); mass spectrum (70 eV) *m/e* (rel intensity) 154 (48, M^+), 139 (100, $M^+ - CH_3$), 136 (85), 111 (88, $M^+ - COCH_3$), 97 (91), 69 (71), 67 (65).

Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.04; H, 6.25.

Procedure B. Distillation of **9a** (7.2 g, 0.025 mol) under reduced pressure afforded 3.3 g of **8a**, yield 86%, bp 99–121° (5 mm).

Addition of 2a to 8a in the Presence of K_2CO_3. The mixed solution of **2a** (0.37 g, 0.0029 mol), **8a** (0.44 g, 0.0029 mol), and potassium carbonate (0.40 g, 0.0029 mol) in 5 ml of water was stirred for 2 hr at 30°. White crystals (0.085 g) precipitated; they were collected, washed with dilute HCl and then with water, and identified as **9a** by comparison of ir spectrum with that of an authentic sample, yield 10%. From the filtrate, 0.59 g of oil was recovered. Alkaline hydrolysis of this oil with 10% NaOH gave 0.14 g of crude terpenylic acid (**11**), yield 27%.

α-Benzoyl-β-benzoylethoxycarbonylmethyl-γ,γ-dimethyl-γ-butyrolactone (9b). To the mixed solution of **2b** (11.5 g, 0.06 mol) and potassium carbonate (8.4 g, 0.06 mol) in 30 ml of water was added 5.3 g (0.05 mol) of **1b** with moderate cooling. After the mixture was stirred for 40 hr at room temperature, for a further 6 hr at 50°, and finally for 1 hr at 60–70°, it was poured into a large amount of water. The product separated as a white solid. It was collected and washed with ether to remove excess of **2b**. One recrystallization of crude product from benzene yielded 11.5 g (94%)[28] of **9b**: mp 133–134°; ir (Nujol) 1754 (lactone C=O), 1727 (ester C=O), 1663 (benzoyl C=O), 1588 and 1572 cm^{-1} (benzene C=C); nmr ($CDCl_3$) δ 0.92 (t, 3, J = 8 Hz, $CO_2CH_2CH_3$), 1.33 (s, 3, CH_3), 1.65 (s, 3, CH_3), 3.83 (q, 2, J = 8 Hz, $CO_2CH_2CH_3$), 4.17 (t, 1, J = 9 Hz, C_β H), 4.65 (d, 1, $>CHCO_2C_2H_5$), 5.23 (d, 1, J = 9 Hz, C_α H), 7.3–8.2 (m, 10, 2 C_6H_5); mass spectrum (70 eV) *m/e* (rel intensity) 216 (17, $M^+ - PhCOCH_2CO_2Et$), 201 (33), 192 (30, $PhCOCH_2CO_2Et$), 173 (38), 170 (28), 158 (85), 146 (35), 106 (60).

Anal. Calcd for $C_{24}H_{24}O_6$: C, 70.58; H, 5.92. Found: C, 70.50; H, 5.96.

Reaction of 2-Hydroxy-2-methylpropanal (1c) with 2b in THF. A solution of **2b** (19.8 g, 0.1 mol), **1c** (8.8 g, 0.1 mol), and potassium carbonate (15.2 g, 0.11 mol) in 30 ml of THF was stirred for 38 hr at room temperature. After work-up of the resulting mixture in the usual manner, 9.8 g of crude **9b** was obtained, yield 48%.

α-Benzoyl-γ,γ-dimethyl-$\Delta^{\alpha,\beta}$-butenolide (8b). Lactone **9b** was distilled at oil-bath temperature (160–170°) under reduced pressure. As the first fraction [bp 101–120° (1.0 mm)], 3.0 g (88%) of **2b** was recovered. As the second fraction [bp 145–150° (1.0 mm)], 2.7 g (71%) of **8b** was obtained. The analytical sample was collected by preparative tlc:[29] mp 65–66°; ir (Nujol) 1750–1780 (lactone C=O), 1650 (benzoyl C=O), 1630 (C=C), 1598 and 1580 cm^{-1} (benzene C=C); nmr ($CDCl_3$) δ 1.58 (s, 6, 2 CH_3), 7.70 (s, 1, =CH), 7.4–7.9 (m, 5, C_6H_5); mass spectrum (70 eV) *m/e* (rel intensity) 216 (2, M^+), 201 (3, $M^+ - CH_3$), 188 (1), 173 (5), 170 (4), 158 (29), 105 (100, PhCO), 77 (57, C_6H_5).

Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.04; H, 5.79.

Addition of 2b to 8b in the Presence of K_2CO_3. A mixture consisting of water (5 ml), potassium carbonate (0.32 g, 0.0023 mol), **2b** (1.0 g, 0.0052 mol), and **8b** (0.4 g, 0.0019 mol) was stirred at room temperature for 20 min and then at 50° for 2 hr. Work-up of the reaction mixture in the usual manner afforded 0.5 g (67%) of white crystals, which were proved to be **9b** by comparison of its infrared spectrum with that of an authentic sample.

γ,γ-Dimethyl-β-phenacyl-γ-butyrolactone (10). The lactone **9b** (1 g, 0.0024 mol) was suspended in aqueous sodium hydroxide which was prepared by dissolving NaOH (2 g, 0.05 mol) in 5 ml of water. After the mixture was stirred for 15 hr at 60°, it was acidified with dilute HCl. The ethereal extract of the organic layer was washed with water and dried over Na_2SO_4. Removal of the solvent left 0.7 g of yellow solid. Tlc analysis[30] of this solid showed two spots at R_f values of 0.25 (component 1) and 0.38 (component 2). Each component was collected by preparative tlc[30] and analyzed. The weight ratio (component 1 to component 2) was 2:3. Component 1 was identified as the lactone **9b** by comparison of its ir spectrum with that of an authentic sample. Component 2 was identified as **10**: yield 73%; mp 97–98°; ir (Nujol) 1750 (lactone C=O), 1683 (benzoyl C=O), 1603 and 1584 cm^{-1} (benzene C=C); nmr ($CDCl_3$) δ 1.34 (s, 3, CH_3), 1.47 (s, 3, CH_3), 1.9–3.3 (m, 5, lactone ring proton and CH_2COPh), 7.3–8.05 (m, 5, C_6H_5); mass spectrum (70 eV) *m/e* (rel intensity) 232 (8, M^+), 217 (19, $M^+ - CH_3$), 214 (12, $M^+ - H_2O$), 203 (1), 174 (12), 146 (49), 105 (100, PhCO), 86 (59), 84 (70), 77 (72, C_6H_5).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.37; H, 7.16.

***dl*-Terpenylic Acid (β-Carboxymethyl-γ,γ-dimethyl-γ-butyrolactone, 11).** Compound **9a** (0.14 g, 0.0005 mol) was hydrolyzed in the same manner as **9b**, using 2 ml of 20% sodium hydroxide. From the ethereal extract, 0.05 g of semisolid material was obtained. Tlc analysis[31] of this material showed that it had 90% purity. The analytical sample collected by preparative tlc was identified as *dl*-terpenylic acid by comparison of its ir and nmr spectra with those of an authentic sample,[4] yield 52%, mp 87° (lit.[4] mp 88–89°).

Registry No.—**1a**, 13206-46-7; **1b**, 917-93-1; **1c**, 20818-81-9; **2a**, 141-97-9; **2b**, 94-02-0; **3a**, 51716-51-9; **3b**, 51716-52-0; **4a**, 51716-53-1; **4b**, 51716-54-2; **5a**, 51716-55-3; **5b**, 51716-56-4; **8a**, 51716-57-5; **8b**, 51716-58-6; **9a**, 51716-59-7; **9b**, 51716-60-0; **10**, 51716-61-1; **11**, 632-04-2.

References and Notes

(1) Presented in part at the 26th Annual Meeting of the Chemical Society of Japan, Hiratsuka, Japan, April 3, 1972, and in part at the 4th International Congress of Heterocyclic Chemistry, Salt Lake City, Utah, July 13, 1973.
(2) A. Takeda, S. Tsuboi, S. Wada, and H. Kato, *Bull. Chem. Soc. Jap.*, **45**, 1217 (1972).
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(5) A. Franke and G. Groeger, *Monatsh. Chem.*, **43**, 55 (1922).
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(7) The ratio of **3a** and **4a** was determined by comparing the intensities of nmr signals at δ 9.62 and 5.29 ppm.
(8) The reaction of **1a** and **2a** in the condition described by Franke, *et al.* (ref 5), brought the analogous result.
(9) This fact provides further evidence to support the 2-hydroxy-2,3-dihydrofuran structure of **4a**.
(10) Lactone **9** is readily decomposed to acylacetate and the butenolide **8** at the oven temperature (180°).
(11) Compound **1a** is transformed to 2-hydroxy-2-methylpropanal: 90% in 15 min, 95% in 30 min, and 97% in 60 min.
(12) α-Halo aldehyde such as 2-chlorononanal, which is hardly converted to 2-hydroxy aldehyde under the same condition, undergoes substitution at the α position followed by cyclization to the corresponding 2-hydroxy-2,3-dihydrofuran derivative (unpublished work).
(13) T. A. Favorskaya and D. A. Shkurgina, *J. Gen. Chem. USSR*, **25**, 713 (1955); *Chem. Abstr.*, **50**, 2427 (1956).
(14) C. L. Stevens and B. T. Gillis, *J. Amer. Chem. Soc.*, **79**, 3448 (1957).
(15) R. Dworzak and J. Pierri, *Monatsh. Chem.*, **52**, 141 (1929).
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(17) Inseparable by tlc: developer, *n*-hexane–acetone (4:1, v/v); R_f 0.40.
(18) The original spectral data were taken just after distillation.
(19) The spectral data were taken 2 weeks after distillation.
(20) Column A: 3 mm o.d. × 2.25 m; temperature, 140°; carrier gas, N_2 (42 ml/min); detector, FID.
(21) After deuterium exchange, nmr showed a singlet at δ 5.36 ppm. Nmr ($CDCl_3$) of crude **4b** also showed a singlet at 5.36 ppm.
(22) This product also underwent the transformation to **4b** quantitatively within 2 weeks after distillation.
(23) Distillation of this oil gave 2.5 g (32%) of **5a**, bp 93–102° (5 mm).
(24) Column B: temperature, 150°; carrier gas, N_2 (42 ml/min); detector, FID.
(25) Column A: temperature, 180°; carrier gas, N_2 (53 ml/min; detector, FID.
(26) The yield based on **2a**.
(27) Because of complicated patterns, it was difficult to interpret this spectrum. Compound **9a** appears to consist of keto and enol tautomers.
(28) The yield based on **2b**.
(29) Developed with *n*-hexane–acetone (3:1, v/v); R_f 0.25.
(30) Developer: *n*-hexane–acetone (3:1, v/v).