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Stereochemical Studies. XLVI.[1] Studies on the Synthesis of 4-Acetoxy-cyclopentane-1,3-dione Derivatives[2]

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As methods for preparing 4-acetoxy-cyclopentane-1,3-dione derivatives (**1**), two synthetic schemes were examined. While the successive catalytic reduction and acetylation of cyclopentane-1,3,4-triones (**2**) according to the reported procedure gave the desired **1**, the acid-catalyzed condensation of O-acetyl malic anhydride (**3**) with isopropenyl acetate (**4a**) and diethyl ketone enol acetate (**4b**) gave 2-carboxymethyl-5-methyl-3-oxo-2,3-dihydrofuran (**6a**) and its 4-methyl derivative (**6b**), respectively, as the sole isolable product. The structures of **6a** and **6b** were elucidated from their chemical and spectroscopic behavior.

Plausible formation mechanism for the compounds was also proposed.

Keywords——reduction of cyclopentane-1,3,4-triones; 4-hydroxy-cyclopentane-1,3-dione derivatives; condensation of O-acetyl-malic anhydride with enol acetates; aluminum chloride; 2-carboxymethyl-3-oxo-2,3-dihydrofurans; fumarylacetone; β-acetoacetylpropionic acetic anhydride intermediates

In connection with our synthetic approaches to optically active natural products containg functionalized cyclopentane and cyclopentene systems,[4] it became necessary for us to synthesize 4-acetoxy-cyclopentane-1,3-dione derivatives (**1**) in their racemic modifications.

Among two reaction schemes which were depicted in Chart 1, the sequential catalytic reduction and acetylation of cyclopentane-1,3,4-triones (**2**) according to the reported method[5] were found to readily afford the desired **1**. However, the attempted preparation of **1** from O-acetyl malic anhydride (**3**) and enol acetates (**4**) by way of 4-acetoxy-2-acyl-cyclopentane-1,3-diones (**5**),[6] simply gave the unexpected cyclization products (**6**).

This report concerns with synthesis of **1** from **2**, reaction of **3** with **4**, and structural elucidation of **6**.

As was reported,[5a–c] the preparation of 4-acetoxy-2-methyl-cyclopentane-1,3-dione (**1b**) was easily accomplished by the catalytic reduction of **2b** (86% yield),[5a,b,7] followed by acetylation with acetic anhydride and pyridine (52% yield).[5a] Treatment of **1b** with excess diazomethane gave the mixture of enol ethers (**7b** and **8b**) which were separable by preparative thin-layer chromatography (TLC). Structures of **7b** and **8b** were assigned by comparing their spectral behavior with those reported.[5a,b]

1) Part XLV: C.C. Tseng, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **25**, 166 (1977).
2) A part of this work was presented at the 95th Annual Meeting of the Pharmaceutical Society of Japan, Nishinomiya, April, 1975.
3) Location: *Hongo, Bunkyo-ku, Tokyo, 113, Japan.*
4) *a*) S. Terashima, *J. Synth. Org. Chem. Japan*, **31**, 353 (1973); *b*) S. Terashima and S. Yamada, *Metabolism and Disease*, **12**, 1489 (1975); *c*) R.A. Ellison, *Synthesis*, **1973**, 397; *d*) T-L, Ho, *Synth. Comm.*, **1974**, 265; *e*) U. Axen, J.E. Pike, and W.P. Schneider, "The Total Synthesis of Natural Products," ed. by J. ApSimon, Wiley-Interscience, New York, London, Sydney, Toronto, 1973, Vol. 1, p. 81.
5) *a*) K. Matoba, K. Yoshii, T. Yamazaki, and Y. Sasaki, *Yakugaku Zasshi*, **89**, 750 (1969); *b*) M. Orchin and L.W. Butz, *J. Am. Chem. Soc.*, **65**, 2296 (1943); *c*) G.D. Searle & Co., Neth. Appl., 6415063 [*C. A.* **64**, 3377*e* (1966)]; *d*) J. Katsube, and M. Matsui, *Agr. Biol. Chem.*, **35**, 401 (1971).
6) *a*) F. Merènyi, and M. Nilsson, *Acta Chem. Scand.*, **17**, 1801 (1963); *b*) *Idem, ibid.*, **18**. 1368 (1964); *c*) V.J. Grenda, G.W. Lindberg, N.L. Wendler, and S.H. Pines, *J. Org. Chem.*, **32**, 1236 (1967); *d*) H. Schick, G. Lehmann, and G. Hilgetag, *Angew. Chem.*, **79**, 97 (1967).
7) "Organic Synthesis," John-Wiley and Sons, Inc., New York, London, 1967, Vol. 47, p. 83.

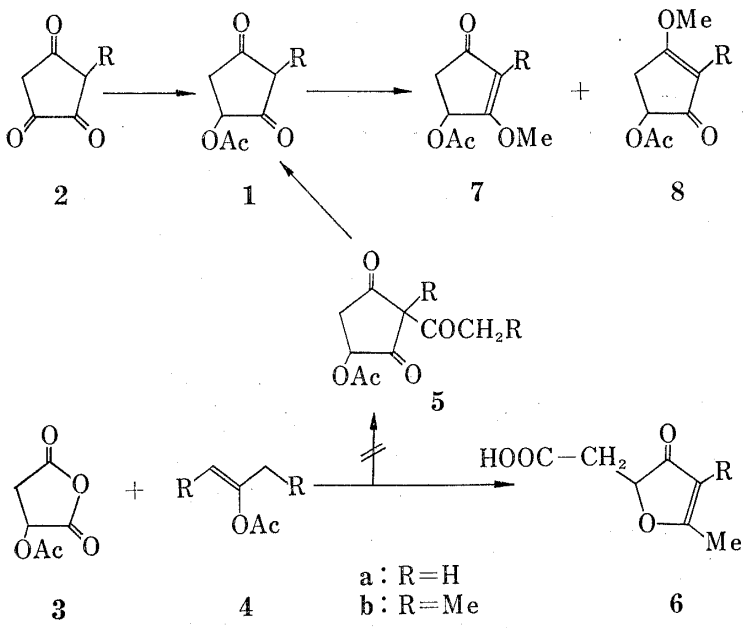


Chart 1

When the above-mentioned reaction scheme was applied to **2a**,[8] 4-acetoxy-cyclopentane-1, 3-dione (**1a**) was obtained as an oil in 46% yield from **2a**. The structure of **1a** was clearly confirmed by converting it into the corresponding crystalline enol ethers (**7a** and **8a**). Assignment of the location of methoxy group in **7a** and **8a** follows from the comparison of their spectral properties with those of **7b** and **8b**.

As a more versatile and direct method for preparing **1**, we next paid attention to the acid-catalized condensation of **3** with **4**, which could afford **1** *via* **5**. As shown in Chart 2, cyclopentane-1,3-dione (**9a**) and its

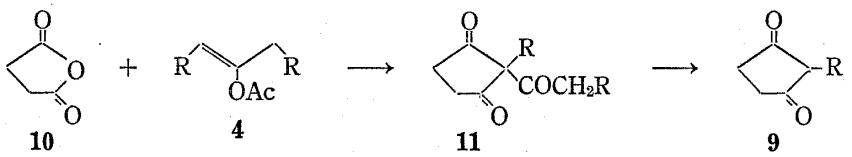


Chart 2

2-methyl analogue (**9b**) have been synthesized from succinic anhydride (**10**) and **4** *via* 2-acylcyclopentane-1,3-diones (**11**) in moderate yields.[6] In some instances,[6c,d] acidic cleavage of the acyl group of **11** occurs during work-up of the condensation product. It was also anticipated that the preparation of optically active **1** (for example (*S*)-**1**) could be achieved by applying the above-cited scheme to the optically active anhydride derived from commercially available (*S*)(−)-malic acid[9] because the chiral center involved in (*S*)(−)-malic acid would not racemize under acidic condition.[10]

The anhydride (**3**)[11] prepared from racemic malic acid, was first treated with anhyd. aluminum chloride (3.0 eq.) in 1,2-dichloroethane, and was allowed to react with **4a** (1.1 eq.). Decomposition of the formed complex with aqueous hydrochloric acid, followed by continuous extraction of the acidic aqueous phase with chloroform and evaporation, gave a complex mixture of the reaction products.[12] Trituration of the evaporation residue with ethyl acetate afforded the crystalline compound (**6a**), mp 146.5—147.5°, as the sole isolable product (20% yield based on **3**).[13]

8) *a*) J.S. Chikos, *J. Org. Chem.*, **38**, 1231 (1973); *b*) J.H. Boothe, R.G. Wilkinson, S. Kushner, and J.H. Williams, *J. Am. Chem. Soc.*, **75**, 1732 (1953).

9) It has been reported that deamination reaction of L-aspartic acid with a combination of sodium nitrite and aqueous sulfuric acid affords (*S*)(−)-malic acid (see for example, B. Iselin, and E.A. Zeller, *Helv. Chim. Acta*, **29**, 1510 (1946)).

10) See for example, J.L. Boomer, and F.E. Kappler, *J. Org. Chem.*, **39**, 113 (1974).

11) S.G. Cohen, Z. Neuwirth, and S.Y. Weinstein, *J. Am. Chem. Soc.*, **88**, 5306 (1966).

12) TLC analysis of this mixture showed more than eight spots (silica gel, solvent benzene: tetrahydrofuran: formic acid 15: 5: 2), whose *Rf* values were 0.82, 0.62, 0.59, 0.52, 0.44, 0.34 (**6a**), 0.22, and 0.12.

13) Isolation of the reaction products other than **6a** was difficult.

The structure of **6a** was determined as 2-carboxymethyl-5-methyl-3-oxo-2,3-dihydrofuran by its spectral properties shown in detail in the experimental part and by its chemical reaction summarized in Chart 3. Ferric chloride test on **6a** exhibited no reddish brown color characteristic to 1,3-dione system. Esterification of **6a** with diazomethane gave the methyl ester (**12a**) as an oil in 82% yield, and catalytic reduction of **6a** over 10% palladium on charcoal[14] proceeded under an atmospheric hydrogen pressure to yield the dihydro derivative (**13a**),[15] mp 96—98°. The ultraviolet (UV) spectrum of **12a** showed an absorption maximum at 262 nm (log ε 4.08 in 95% ethanol) which was very close to that of 2, 5-dimethyl-3-oxo-2 ,3-dihydrofuran ($\lambda_{max}^{ethanol}$ 260 nm (log ε 4.09)).[16] Carbon-13 nuclear magnetic resonance (NMR) spectrum[17] of **12a** showed a good accordance with the assigned structure (see experimental). Treatment of **6a** with potassium hydroxide in methanol at room temperature, gave fumarylacetone (**14**) in 50% yield, which was identified with the authentic sample independently prepared from maleic anhydride and **4a**

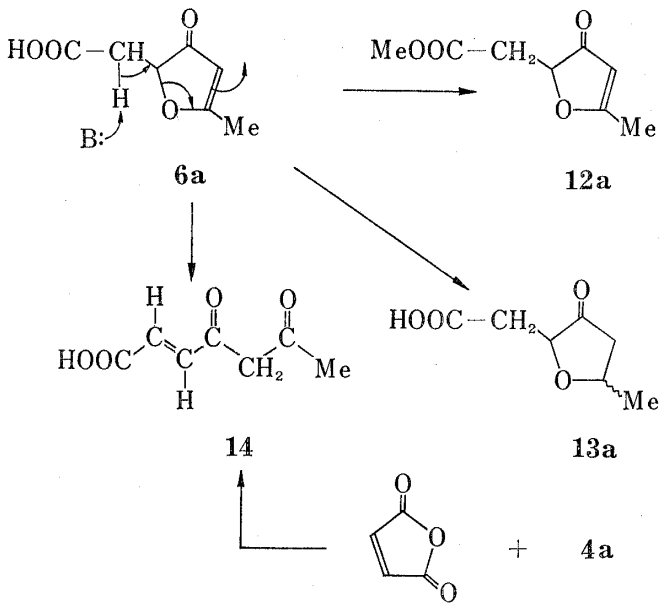


Chart 3

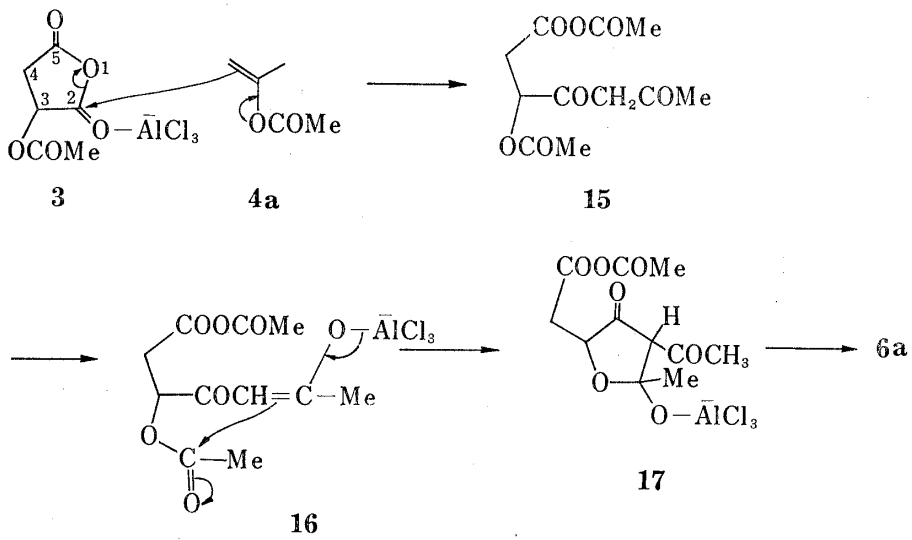


Chart 4

14) It has been reported that 3-oxo-2,3-dihydrofuran system can be readily reduced on catalytic hydrogenation with palladium on charcoal (C.H. Eugster, *Helv. Chim. Acta*, **40**, 2462 (1957), and C.H. Eugster, F. Häflinger, R. Denss, and E. Girod, *ibid.*, **41**, 205 (1958)).

15) Although formation of *cis*- and *trans*-isomers is theoretically possible for this reduction due to the direction of hydrogen attack, one isomer, whose relative configuration at C_2- and C_5-positions could not be determined by its spectral data, was obtained by the repeated recrystallizations from a mixture of ether and hexane.

16) "Organic Electronic Spectral Data," ed. by J.P. Phillips, R.E. Lyle, and P.R. Jones, Interscience Publishers, Inc., New York, London, Sydney, Toronto, 1969, Vol. V., p. 71.

17) Authors are indebted to Dr. M. Matsuo, Tokyo Metropolitan Institute of Gerontology, for measuring this spectrum.

according to the reported method.[18] Formation of **14** from **6a** might be construed by the mechanism shown in Chart 3 (**6a**, arrows).

Although the reaction mechanism for the condensation of **10** with **4** which can give **9** *via* **11**, has not been fully elucidated, β-acetoacetylpropionic acetic anhydride is presented as a possible intermediate.[6b] It is quite ambiguous the reason why **6a** could be produced from **3** and **4a**, but one mechanistic explanation shown in Chart 4, might coincide with the observed result. The attack of **4a** to the activated carbonyl gronp of **3** (C_2-position) can afford the similar anhydride (**15**) to that for the reaction with **10**, and the active methylene of **15** reacts with the intramolecular acetoxy group instead of the anhydride group (as depicted in **16**), giving the cyclized complex (**17**). Decomposition of **17** during the reaction and/or the aqueous work-up yields **6a**.[19]

When the condensation was examined by using **3** and diethyl ketone enol acetate (**4b**) under a similar reaction condition to that for **4a**, 2-carboxymethyl-4,5-dimethyl-3-oxo-2,3-dihydrofuran (**6b**), mp 113—115°, was obtained in 17% yield as the isolable crystalline product. The structure of **6b** was determined by the comparison of its spectral behavior with those of **6a**. This observation might further support the formation mechanism shown in Chart 4.

Further studies which aim to prepare cyclopentane-1,3-dione skeleton from malic acid derivatives, are still under progress.

Experimental[20]

4-Acetoxy-3-methoxy-2-methyl-2-cyclopentenone (7b) and 5-Acetoxy-3-methoxy-2-methyl-2-cyclopentenone (8b)——Treatment of **1b** (mp 110—112°)[5a,b,7] (0.17 g, 1.0 mmole) with an ethereal solution of diazomethane, followed by the usual work-up, gave a crude mixture of **7b** and **8b** as an oil (185 mg). TLC analysis (silica gel, solvent ether: hexane 2: 1) of this oil showed two spots whose *Rf* values were 0.35 and 0.19. Separation by preparative TLC (silica gel, solvent ether: hexane 2: 1) gave oily **7b** (*Rf* 0.35) (73 mg, 40%) and **8b** (*Rf* 0.19) (75 mg, 41%). Structures of **7b** and **8b** were determined by comparing their spectral (NMR and UV) data with those reported.[5a,d]

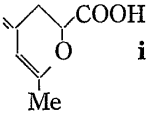
7b: IR ν_{max}^{film} cm^{-1}: 1747, 1705, 1645. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1747. 1703, 1640. NMR (in $CDCl_3$): 1.72 (3H, nearly s, =C–C$\underline{H}_3$), 2.10 (3H, s, COC$\underline{H}_3$), 2.20 (1H, dd, J=18, 2 Hz, one of C$\underline{H}_2$CHO), 2.88 (1H, dd, J=18, 6 Hz, one of C$\underline{H}_2$CHO), 3.99 (3H, s, OC$\underline{H}_3$), 5.70 (1H, dm, J=6 Hz, $CH_2C\underline{H}O$). Homoallylic coupling was observed for the signals at 1.72 and 5.70 ppm the same as that reported.[5a,d] UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 250 (4.18).

8b: IR ν_{max}^{film} cm^{-1}: 1750, 1710, 1630. NMR (in $CDCl_3$): 1.59 (3H, nearly s, =C–C$\underline{H}_3$), 2.08 (3H, s, CO-C$\underline{H}_3$), 2.48 (1H, dm, J=18 Hz, one of C$\underline{H}_2$CHO), 3.21 (1H, dm, J=18 Hz, one of C$\underline{H}_2$CHO), 3.94 (3H, s, O-C$\underline{H}_3$), 5.10 (1H, dd, J=7, 3 Hz, $CH_2C\underline{H}O$). The same homoallylic coupling as that reported[5d] was observed for the signals at 1.59 and 2.48, 3.21 ppm. UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 259 (4.08). Difference of the UV spectra between **7b** and **8b** was similar to that observed for 4-hydroxy-3-methoxy-2-propyl-2-cyclopentenone (UV λ_{max}^{EtOH} nm: 252) and 5-hydroxy-3-methoxy-2-propyl-2-cyclopentenone (UV λ_{max}^{EtOH} nm: 256).[5d]

4-Acetoxy-cyclopentane-1,3-dione (1a)——A solution of **2a**,[8a] mp 167.5—169.5° (decomp.)(lit.,[8a] mp 172—174° (decomp.); lit.,[8b] mp 172.5—173° with decomposition starting at 167°), (0.87 g, 7.8 mmole) and 10% Pd/C (0.30 g) in a mixture of isopropanol and H_2O (4: 1) (30 ml) was stirred at room temperature for 2 hr

18) *a*) M. Nilsson, *Acta Chem. Scand.*, **18**, 441 (1964); *b*) J. Fowler and S. Seltzer, *J. Org. Chem.*, **35**, 3529(1970).

19) Considering the other possible mode of the attack of **4a** to the activated carbonyl group of 3(C_5-position), it is probable that 2-carboxy-4-oxo-6-methyl-2,3-dihydropyran(**i**) might be prepared, following to a similar reaction course to that for **6a**. Although the formation of **i** was spectroscopically observed, its isolation in a pure state has not been achieved.



i

20) All melting points are uncorrected. Infrared (IR) spectra were measured with spectrometers, JASCO Infrared Spectrometer Model DS-402G and JASCO IRA-1 Grating Infrared Spectrometer. Proton NMR spectra were recorded with spectrometers, JNM-PS 100 and Hitachi R-24 High Resolution NMR Spectrometers. All signals are expressed by the ppm downfield from tetramethylsilane used as an internal standard. Following abbreviations are used: singlet (s), doublet(d), triplet(t), quartet(q), multiplet(m), and broad(br). UV spectra measurements are carried out with a spectrometer, Model EPS-3T, Hitachi Recording Spectrometer. Measurements of mass spectra were performed using a JEOL JMS-01 SG-2 Mass Spectrometer.

under hydrogen atmosphere. Filtration and evaporation *in vacuo* gave crude 4-hydroxy-cyclopentane-1,3-dione (1.11 g) as a pale yellow oil. IR ν_{max}^{film} cm^{-1}: 1655, 1580. This sample was directly submitted to the next acetylation.

Acetic anhydride (3.0 ml) was gradually added to a stirred solution of crude 4-hydroxy-cyclopentane-1,3-dione (0.63 g, 5.6 mmole) in pyridine (6 ml) in an ice bath. After stirring was continued at 0° for 1 hr, 10% aqueous HCl solution (20 ml) was added to the reaction mixture, and the whole solution was extracted with ethyl acetate (20 ml × 4). Combined organic extracts were successively washed with 10% aqueous HCl (20 ml × 2), and satd. NaCl solutions, and finally dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* afforded an orange oil, which was dissolved in H_2O (40 ml) and treated with charcoal. Filtration and evaporation *in vacuo*, gave an oily residue. Addition of chloroform (20 ml) to the residue, followed by evaporation *in vacuo*, was repeated three times to remove H_2O to give crude **1a** as an orange oil (0.32 g, 46% based on **2a**). IR ν_{max}^{film} cm^{-1}: 1745, 1660, 1570. NMR (in $CDCl_3$): 2.13 (3H, s, $COCH_3$), 2.50 (1H, dd, J=18, 3 Hz, one of CH_2CHO). 3.08 (1H, dd, J=18, 6 Hz, one of CH_2CHO), 5.46 (1H, s, CH=C–OH), 5.60 (1H, dd, J=6,3 Hz, CH_2CHO), 11.44 (1H, s, CH=C–OH). UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 242 (4.12). Mass Spectrum *m/e*: 156 (M^+), 114, 96, 87, 86, 85, 84, 83, 69, 55, 49, 48, 47, 43. TLC analysis of this sample showed one main spot (*Rf ca.* 0.3) and three small spots due to impurities at *Rf ca.* 0.5, 0.1, and 0.03 (silica gel, solvent benzene: tetrahydrofuran: formic acid 15: 5: 2).

4-Acetoxy-3-methoxy-2-cyclopentenone (7a) and 5-Acetoxy-3-methoxy-2-cyclopentenone (8a)——Similar treatment of crude **1a** (0.40 g, 2.7 mmole) to that of **1b** gave a crude mixture of **7a** and **8a** as a pale yellow oil (0.25 g). TLC analysis of this oil showed two main spots at *Rf* 0.36 and 0.28 (silica gel, solvent ether: hexane 3: 1, 3 developments). Purification by preparative TLC (silica gel, solvent ether: hexane 3: 1, 4 developments) gave crude **7a** (*Rf* 0.36) (0.12 g, 26%), mp 75—77°, and **8a** (*Rf* 0.28) (0.08 g, 18%), mp 32—43°.

7a: Recrystallization from ether–hexane gave pure **7a** as colorless crystals, mp 78.5—79.5°. IR ν_{max}^{Nujol} cm^{-1}: 1743, 1719, 1620. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1746, 1716, 1611. NMR (in $CDCl_3$): 2.10 (3H, s, $COCH_3$), 2.35 (1H, dd, J=18, 2 Hz, one of CH_2CHO), 2.86 (1H, dd, J=18, 7 Hz, one of CH_2CHO), 3.87 (3H, s, OCH_3), 5.41 (1H, s, CH=C), 5.75 (1H, dd, J=7, 2 Hz, CH_2CHO). UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 235 (4.32). Mass Spectrum *m/e*: 170 (M^+), 128, 127, 111, 87, 83, 69, 59, 43. *Anal.* Calcd. for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.48; H, 5.94.

8a: Recrystallization from ether–hexane gave pure **8a** as a colorless powder, mp 45.5—46.5°. IR ν_{max}^{Nujol} cm^{-1}: 1745, 1698, 1596. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1746, 1712, 1595. NMR (in $CDCl_3$): 2.11 (3H, s, $COCH_3$), 2.50 (1H, dd, J=18, 3 Hz, one of CH_2CHO), 3.08 (1H, dd, J=18, 7 Hz, one of CH_2CHO), 3.86 (3H, s, OCH_3), 5.18 (1H, dd, J=7, 3 Hz, CH_2CHO), 5.34 (1H, br s. CH=C). The signal at 5.34 ppm showed a weak allylic coupling with the signals at 2.50 and 3.08 ppm. UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 242 (4.25). Mass Spectrum *m/e*: 170 (M^+), 128, 127, 111, 110, 99, 95, 83, 69, 67, 43. Spectral differences (IR, NMR, and UV) between **7a** and **8a** were similar to those observed for **7b** and **8b**. *Anal.* Calcd. for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.51; H, 5.96.

O-Acetyl Malic Anhydride (3)——Prepared according to the reported procedure,[11] and recrystallized from toluene, prisms, mp 81.5—82.5° (lit.,[11] mp 86—87°). IR ν_{max}^{Nujol} cm^{-1}: 1880, 1800, 1748. NMR (in $CDCl_3$): 2.16 (3H, s, $COCH_3$), 2.92 (1H, dd, J=18, 7 Hz, one of CH_2CHO), 3.32 (1H, dd, J=18, 9 Hz, one of CH_2CHO), 5.45 (1H, dd, J=9, 7 Hz, CH_2CHO).

2-Carboxymethyl-5-methyl-3-oxo-2,3-dihydrofuran (6a)——To a suspension of finely-powdered anhyd. aluminum chloride (20.0 g, 0.150 mole) in 1,2-dichloroethane (100 ml) was added 3 (7.90 g, 0.050 mole) with stirring. The mixture was stirred at room temperature for 1 hr to give a clear colorless solution, which was cooled to −10° in a dryice-CCl_4 bath. A solution of **4a** (5.50 g, 0.055 mole) in 1,2-dichloroethane (50 ml) was gradually added to the cooled solution, and the whole solution was stirred for 2 hr in an ice bath, overnight at room temperature, and finally for 2 hr at 65—70°. After cooling, a mixture of conc. HCl and H_2O (1: 5) (100 ml) was added to the reaction mixture to decompose the formed complex, and the lower organic phase was separated. The upper acidic aqueous layer was submitted to successive extraction using chloroform for 6 hr. The chloroform extract was evaporated *in vacuo* to give a mixture of white powder and orange oil (6.42 g). TLC analysis of this mixture showed more than eight spots.[12] Trituration with ethyl acetate (4.5 ml), followed by filtration and drying, afforded crude **6a** as a pale yellow powder (1.36 g), mp 143—145°. Evaporation of the ethyl acetate mother liquor *in vacuo* gave an orange oil (4.76 g), which precipitated further amount of **6a**. Filtration and washing with ethyl acetate gave further amount of crude **6a** as a pale yellow powder (0.21 g, total 1.57 g, 20%), mp 142—143.5°. Repeated recrystallizations of crude **6a** from ethyl acetate gave pure **6a** as colorless prisms, mp 146.5—147.5°. IR ν_{max}^{Nujol} cm^{-1}: 1749, 1633, 1600. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1748, 1668, 1616. NMR (in methanol-d_4): 2.07 (3H, s, =C–CH_3), 2.75 (2H, d, J=7 Hz, CH_2CHO), 5.07 (1H, t, J=7 Hz, CH_2CHO), 5.21 (1H, s, $COCH$=C–CH_3), 10—12 (1H, br s, COOH). The signal at 10—12 ppm disappeared on D_2O treatment. UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 2.66 (4.09). Mass Spectrum *m/e*: 156, 122, 112, 111, 85, 84, 71, 69, 55, 43. *Anal.* Calcd. for $C_7H_8O_4$: C, 53.84; H, 5.16. Found: C, 53.78; H, 5.25.

2-Methoxycarbonylmethyl-5-methyl-3-oxo-2,3-dihydrofuran (12a)——An ethereal solution of diazomethane was added to a suspension of **6a** (0.50 g, 3.2 mmole) in ether (5 ml) until the yellow color of diazomethane remained. An excess amount of diazomethane was decomposed by the addition of acetic acid, and the whole mixture was washed with satd. $NaHCO_3$ (×2), then dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* afforded pure **12a** as a pale yellow oil (0.45 g, 82%). TLC analysis of this oil showed a single spot whose *Rf* value was 0.38 (silica gel, solvent ether: hexane 3: 1, 2 developments). IR ν_{max}^{film} cm^{-1}: 1760, 1669,

1616. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1762, 1665, 1617. NMR (in $CDCl_3$): 2.10 (3H, s, =C–C$\underline{H}_3$), 2.76 (2H, d, J=8 Hz, C$\underline{H}_2$-CHO), 3.80 (3H, s, OC$\underline{H}_3$), 5.02 (1H, t, J=8 Hz, $CH_2C\underline{H}O$), 5.32 (1H, s, COC$\underline{H}$=). UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 262 (4.08). Mass Spectrum *m/e*: 170 (M^+), 142, 127, 111, 110, 87, 85, 84, 71, 69, 55, 43. ^{13}C-NMR (25.2 MHz, in $CDCl_3$):[21] 21.0 (=C–$\underline{C}H_3$), 37.4 ($\underline{C}H_2CH$), 52.9 ($\underline{C}H_3OCO$), 76.2 ($CH_2\underline{C}HO$), 106.1 (CO$\underline{C}$H=C), 169.1 (=$\underline{C}$–CH_3 or $CH_3O\underline{C}O$), 173.5 (=$\underline{C}$–CH_3 or $CH_3O\underline{C}O$), 189.8 (CH$\underline{C}$OCH=).

2-Carboxymethyl-5-methyl-3-oxo-tetrahydrofuran (13a)——A mixture of **6a** (0.10 g, 0.64 mmole) and 10% Pd/C (0.04 g) in anhyd. tetrahydrofuran (8 ml) was stirred at 0° under hydrogen atmosphere for 3.5 hr. TLC analysis of the mixture clearly showed that **6a** (*Rf* 0.28) completely disappeared and a new spot appeared at *Rf* 0.35 (silica gel, solvent benzene: tetrahydrofuran: formic acid 15: 5: 2). Filtration and evaporation *in vacuo* gave a colorless oil (0.09 g), which gradually solidified on standing. Repeated recrystallizations from ether–hexane gave pure **13a** as colorless needles, mp 96—98°. IR ν_{max}^{Nujol} cm^{-1}: 1750, 1680. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1731. NMR (in $CDCl_3$): 1.45 (3H, d, J=6 Hz, CH–C$\underline{H}_3$), 1.90—3.02 (4H, m, OCOC$\underline{H}_2$CHO and COC$\underline{H}_2$CH-CH_3), 3.84 (1H, m, $CH_2C\underline{H}CH_3$), 4.33 (1H, dd, J=10, 4 Hz, $CH_2C\underline{H}O$), 7.71 (1H, s, COOH). Mass Spectrum ***m/e*: 158** (M^+), 149, 140, 113, 73, 71, 69, 55, 45, 43, 42, 41. *Anal.* Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.44; H, 6.42.

Fumarylacetone (14)——a) **14** from Maleic Anhydride: This compound was prepared as almost colorless long needles (recrystallized from benzene) according to the reported procedure,[18a] and showed mp 164.5—166° (lit.,[18a] mp 158—160°; lit.,[18b] mp 162—166°). Spectral data of this compound were identical with those reported.[18] IR ν_{max}^{KBr} cm^{-1}: 1685, 1645, 1598. NMR (in acetone-d_6): 2.21 (3H, s, COC$\underline{H}_3$), 6.01 (1H, s, CO–C$\underline{H}$–CO), 6.83 (2H, AB type q, J=16 Hz, olefinic protons), 4.00—7.00 (2H, br s, COO$\underline{H}$ and O$\underline{H}$).

b) **14** from **6a**: A mixture of **6a** (0.16 g, 1.0 mmole) and KOH (0.17 g, 3.0 mmole) in methanol (2 ml) was stirred at room temperature for 6 hr, giving a yellow solution containing a colorless powder. After the whole solution was acidified to pH 3 with 12% aqueous HCl solution, it was diluted with ethyl acetate (20 ml), and dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo*, gave a yellow residue which was recrystallized from benzene to give **14** as faint yellow long needles (0.08 g, 50%), mp 163—164.5°. Further recrystallization from benzene gave pure **14** as almost colorless long needles, mp 163.5—164.5°. Spectral (IR and NMR) and chromatographic (TLC) behavior of this sample were completely identical with those of the authentic **14**. This sample showed no depression on the mixed melting point measurement with the authentic **14** (mp 164.5—166°).

2-Carboxymethyl-4,5-dimethyl-3-oxo-2,3-dihydrofuran (6b)——To a suspension of finely powdered anhyd. aluminum chloride (8.0 g, 0.060 mole) in 1,2-dichloroethane (25 ml), was added **3** (3.16 g, 0.020 mole) with stirring. The mixture was further stirred at room temperature for 2 hr, then cooled in a dryice-CCl_4 bath. A solution of **4b** (3.03 g, 0.024 mole) in 1,2-dichloroethane (5 ml) was gradually added to the cooled solution, and the whole was treated in a similar manner to the case for **6a**, affording an orange oil (2.40 g) after evaporation of the chloroform extract. Trituration of the oil with a mixture of benzene and ethyl acetate, followed by filtration of the separated powder and drying, gave crude **6b** as a crystalline solid (0.58 g, 17%), mp 107—109°. Repeated recrystallizations from benzene afforded pure **6b** as colorless crystals, mp 113—115°. IR ν_{max}^{Nujol} cm^{-1}: 1740, 1620, 1575. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1660, 1615. NMR (in $CDCl_3$): 1.70 (3H, s, COC–C$\underline{H}_3$), 2.10 (3H, s COC=C–C$\underline{H}_3$), 2.86 (2H, d, J=7 Hz, C$\underline{H}_2$CHO), 4.98 (1H, t, J=7 Hz, CH_2-C$\underline{H}$O), 10.9 (1H, s, COO$\underline{H}$). UV $\lambda_{max}^{95\%\ EtOH}$ nm: (log ε): 275 (4.08). Mass Spectrum *m/e*: 170 (M^+), 125, 98, 83, 70, 56, 43. *Anal.* Calcd. for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.46; H, 5.90.

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21) Measured with a spectrometer, Varian XL-100.