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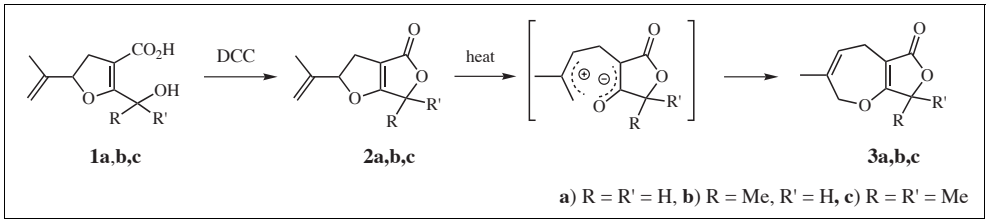

Lactonization of 2-(hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylic acids **1a,b,c** with dicyclohexylcarbodiimide gave the corresponding furano-lactones, 5-isopropenyl-5,6-dihydro-1(3*H*)-furo[3,4-*b*]furanone **2a,b,c**, which were readily converted to the corresponding oxepino-lactones, 6-methyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone **3a,b,c** by respective thermal ring expansions.

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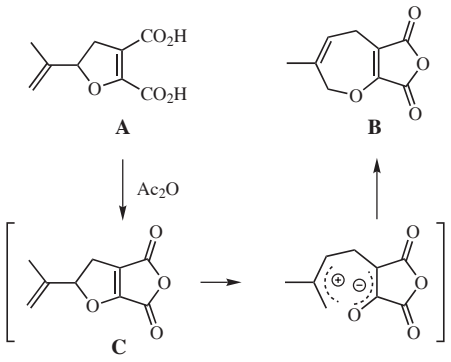
In our previous paper we reported a ring expansion of 5-isopropenyl-4,5-dihydrofuran-2,3-dicarboxylic acid (**A**) giving 6-methyl-4,7-dihydroxepin-2,3-dicarboxylic anhydride (**B**) [1], as shown in Scheme 1. It is thought that this ring expansion might be caused by the ring strain due to the 5-5 fused ring system in 5-isopropenyl-4,5-dihydrofuran-2,3-dicarboxylic anhydride (**C**), which might be formed through anhydride formation.

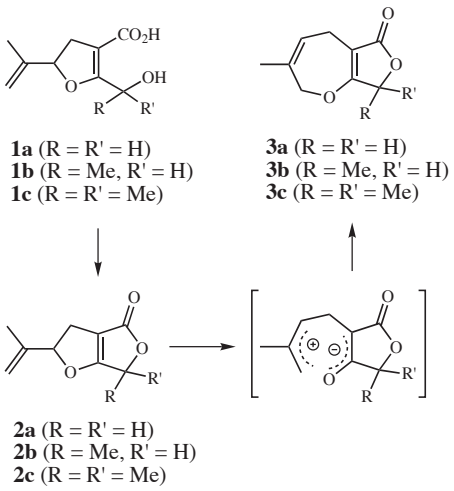
Scheme 1



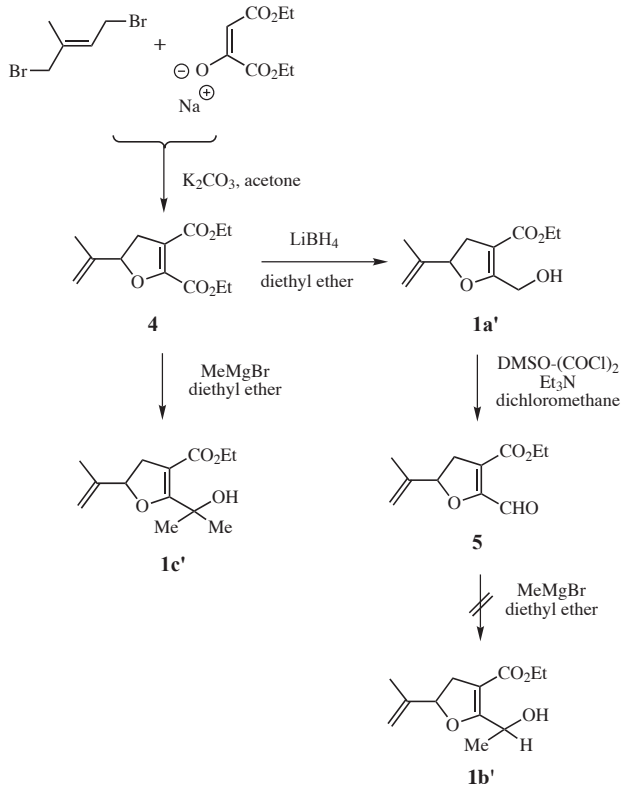
In this paper, we describe a similar ring expansion in the lactone formation of some 2-(hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylic acids (**1**) giving corresponding 3-methyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinones (**3**)[2] *via* 2-isopropenyl-3,6-dihydro-4(2*H*)-furo-[3,4-*b*]furanones (**2**).

In accordance with the reported procedure [3], the starting material, diethyl 5-isopropenyl-4,5-dihydrofuran-2,3-dicarboxylate (**4**) was prepared through condensation of diethyl oxaloacetate with (*E*)-1,4-dibromo-2-methyl-2-butene. As describe in our previous paper [3], Grignard methylation of diester **4** with excess methylmagnesium bromide gave a half ester, ethyl 2-(1-hydroxy-1-methylethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxyl-ate (**1c**). This showed that the carbonyl might be inert for any nucleophile. Reduction of diester **4** with lithium borohydride gave another half ester, ethyl 2-(hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carb-oxylate (**1a'**). For an approach to the third half ester, ethyl 2-(1-hydroxyethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1b'**), **1a'** was oxidized under Swern condition to ethyl 2-formyl-5-isopropenyl-4,5-dihydro-furan-3-carboxylate (**5**), and then **5** was subjected to Grignard methylation. However, the Grignard methylation of **5** with methylmagnesium bromide caused decomposition of the furan ring in any condition.

Scheme 2

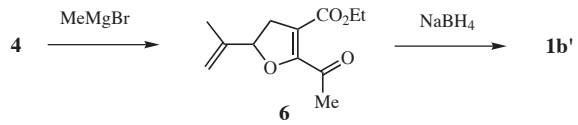


Scheme 3



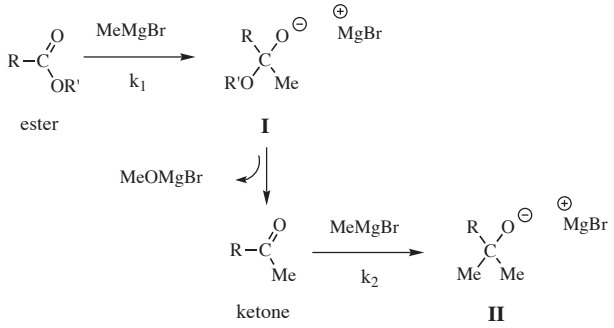
Next, for another approach for **1b'**, as shown in Scheme 4, the Grignard methylation of diester **4** giving ethyl 2-acetyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylate **6** and a following reduction was planned. Normal Grignard methylation of **4** with equimolar methylmagnesium bromide in dry diethyl ether gave a mixture of dimethyl alcohol **1c'** (40%) and starting diester **4** (13%) at room temperature. These double alkylations are normal for the common esters.

Scheme 4



In the usual Grignard reaction of a common ester, as shown in Scheme 5, the first attack of methylmagnesium bromide forms magnesium α-alkyl-α-alkoxyethanoate **I**, which readily converts to the corresponding alkyl methyl ketone, and the second attack forms α-alkyl-α-methyl-ethanoate **II**. Usually, the second attack is faster than the first attack.

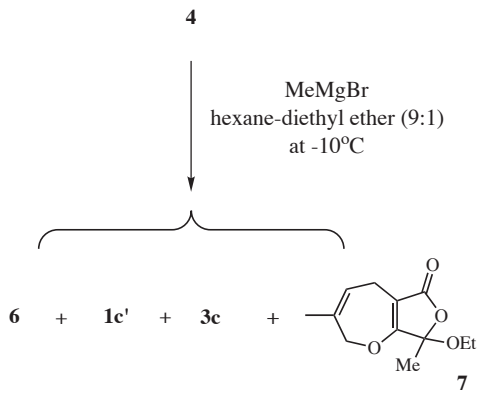
Scheme 5



To prevent the second attack, the Grignard methylation of **4** with equimolar methylmagnesium bromide was studied under a low temperature or in a less polar solvent. The Grignard methylation under a low temperature (at -10°C) gave a mixture of dimethyl alcohol **1c'** (44%) and the desired **6** (22%). In this condition (under a low temperature of –10°C), the migration of magnesium alkoxide ion from the magnesium furanyl-methoxylethanolate **I'** (corresponded to **I**; insoluble to diethyl ether) to afford the corresponding furanyl methyl ketone **6** (soluble to diethyl ether) was reduced, and an aquouse quenching converts alkoxide **I'**, to furanyl methyl ketone **6**.

A similar Grignard methylation of **4** in diethyl ether-hexane (1:4) at –10°C gave the desired **6** (26%), and, as shown in Scheme 6, dimethyl alcohol **1c'** (10%) and two dihydro-1(3*H*)-furo[3,4-*b*]oxepinone **3c** (3%) and **7** (1%) were also obtained as minor components. In this condition (in less polar solvent under a low temperature of –10°C), the solubility of the magnesium furanylmethoxylethanolate **I'** was reduced in the reaction medium, and the conversion to the furanyl methyl ketone **6** was also reduced.

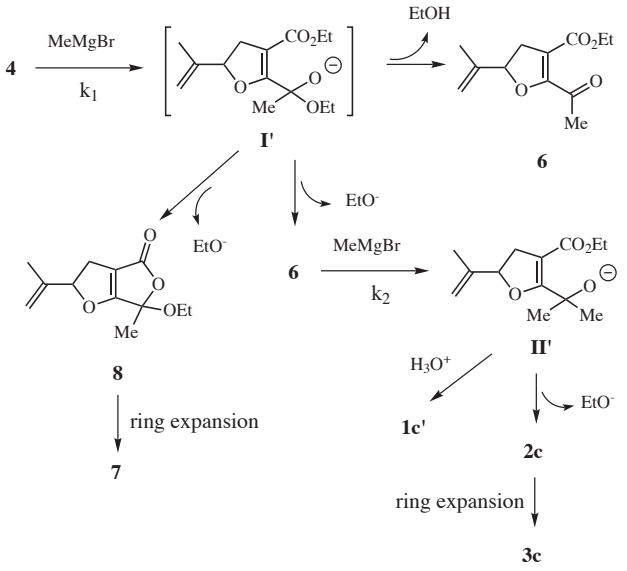
Scheme 6



Two dihydrofuroxepinones **3c** and **7** might be formed by lactonization of corresponding isopropenylfuro-

furanones **2c** and **8**, which were derived from furanyl methyl ethoxide or ethoxyl furanyl ethoxide, followed by ring expansion. These showed the ring expansion occurred under mild conditions (at –10°C).

Scheme 7



The furanyl methyl ketone **6**, thus obtained, was then reduced with sodium borohydride to give ethyl 2-(1-hydroxyethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate **1b'**.

The three half esters **1a',b',c'**, thus obtained, were then converted to the corresponding 2-(hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylic acids (**1a,b,c**) by respective alkalin hydrolyses.

The lactonization of **1a,b,c** by treating with dicyclohexylcarbodiimide gave the corresponding isopropenyldihydrofurofuranones **2a,b,c**, showing an ABX pattern in the pmr. It was very interesting that no ring expansion was observed in the lactonization of **1a,b,c**, but the ring expansion was observed in the lactonization of **I'** (*via* **8**) and **II'** (*via* **2c**) even under mild conditions.

The isopropenyldihydrofurofuranones **2a,b,c**, thus obtained were subjected to thermal ring expansion, and isopropenyldihydrofurofuranones **2a,b** caused ring expansion at 100°C for 1 hour to give the corresponding 3-methyl-3,6-dihydro-4(2*H*)-furo[3,4-*b*]furanones **3a,b**, but **2c** showed no ring expansion under a similar temperature, and was caused by heating at 120°C for 30 min to give **3c**.

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agents and distilled before use. Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Microanalyses were performed on a Yanako MT-5 Elemental Analyser. The ir spectra were recorded on a Jasco ft-ir 7300 spectrophotometer, in potassium bromide disks or liquid films. The ^{1}H and ^{13}C nmr spectra were recorded on a Jeol A-400 or a Mac-FX-90 nmr spectrometer in deuteriochloroform solutions with TMS as internal standard. The mass spectra were recorded on a Jeol JMS-OISG-2- spectrometer in Electron Ionization methods.

Lithium Borohydride Reduction of Diethyl 5-Isopropenyl-4,5-dihydrofuran-2,3-dicarboxylate (**4**).

To a solution of diethyl 5-isopropenyl-4,5-dihydrofuran-2,3-dicarboxylate (**4**) (1.50 g, 5.90 mmoles) in dry diethyl ether (50 ml) was added a solution of lithium borohydride (65 mg, 3.0 mmol) in dry diethyl ether (10 ml), and the mixture was stirred at room temperature for 1 h. After treating with a saturated aqueous ammonium chloride solution and saturating with sodium chloride, the mixture was extracted with diethyl ether. The ether layer was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residual oil was chromatogramed on a silica-gel column eluting with hexane-ethyl acetate (85:15) to give the recovered starting material (753 mg, 49%) and ethyl 2-(hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1a'**) (421 mg, 33%, revised 65%).

Ethyl 2-(Hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1a'**), bp 135-150 °C; ir (liquid film): 3452 (OH), 1698 cm^{-1} (C=O); ^{1}H nmr ($CDCl_3$): δ 1.3 (*t*, J = 7.0 Hz, 3H, $-CO_2CH_2CH_3$), 1.8 (br s, 3H, Me in isopropenyl), 2.5-3.0 (broad s, 1H, OH), 2.7 (dd, J = 9.0, 15.4 Hz, 1H, 4-H_AH_B), 3.1 (dd, J = 10.5, 15.4 Hz, 1H, 4-H_AH_B), 4.2 (q, J = 7.0 Hz, 2H, $-CO_2CH_2CH_3$), 4.4 (br s, 2H, $-CH_2OH$), 4.9 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.2 ppm (dd, J = 9.0, 10.5 Hz, 1H, 5-H_X); mass 212 (M^+), 183 (M^+-Et), 153 (M^+-CO_2Et).

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.97; H, 7.82.

Swern Oxidation of Ethyl 2-(Hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1a'**).

Under an argon atmosphere, to a solution of dimethyl sulfoxide (0.17 ml, 2.39 mmoles) in dichloromethane (2 ml) was cooled at –78 °C, and oxalyl chloride (0.20 ml, 2.3 mmol) was added to the mixture, and the mixture was stirred at –78 °C for 45 minutes. A solution of ethyl 2-(hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1a'**) (155 mg, 0.72 mmol), triethylamine (0.66 ml, 4.7 mmol) in dry dichloromethane (5 ml) was added to the mixture, and the mixture was stirred at –78 °C for 1 hour, and allowed to warm to 0 °C. After treating with water (20 ml) for 5 minutes, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was purified on a silica-gel column to give ethyl 2-formyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**5**)(143 mg, 94%) as the fractions eluted with benzene-ethyl acetate (19:1).

Ethyl 2-Formyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**5**), bp 150-160 °C (3 mmHg)(bath tem); ir (liquid flim): 1703 (CHO), 1693 cm^{-1} (CO_2Et); ^{1}H nmr ($CDCl_3$): δ 1.3 (*t*, J = 7.0 Hz, 3H, $-CO_2CH_2CH_3$), 1.8 (br s, 3H, Me in isopropenyl), 2.9 (dd, J = 9.4, 17.6 Hz, 1H, 4-H_AH_B), 3.3 (dd, J = 10.6, 17.6

Hz, 1H, 4-H_AH_B), 4.3 (q, J = 7.0 Hz, 2H, -$CO_2CH_2CH_3$), 4.9 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.3 (dd, J = 9.4, 10.6Hz, 1H, 5-H_X), 10.3 ppm (s, 1H, CHO); mass 210 (M^+), 181 (M^+-Et), 151 (M^+-CO_2Et).

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.84; H, 6.73. Found: C, 62.93; H, 6.81.

Grignard Alkylation of Diester **4** with Methylmagnesium bromide.

With Excess molar MeMgBr at Room Temp)

Under an argon atmosphere, to a solution of **4** (1.60 g, 6.30 mmol) in dry diethyl ether (40 ml) was added 1.0 M methylmagnesium bromide diethyl ether solution (6.4 ml, 6.4 mmol), and the mixture was stirred at room temperature for 1 hour. After treating with saturated aqueous ammonium chloride solution, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was chromatogramed on a silica-gel column. Starting diester **4** (512 mg, 32%) was recovered as the fractions eluted with hexane-ethyl acetate (95:5). Ethyl 2-(1-hydroxy-1-methylethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate **1c'** (620 mg, 41%, revised 80%) was obtained as the fractions eluted with hexane-ethyl acetate (98:2).

Ethyl 2-(1-Hydroxy-1-methylethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate **1c'**, bp *ca.* 110 °C (18 mmHg)(bath temperature); ir (liquid flim): 3350 (OH), 1670 cm^{-1} (CO_2Et); ^{1}H nmr ($CDCl_3$): δ 1.3 (s, 6H, two Me), 1.3 (*t*, J = 7.0 Hz, 3H, -$CO_2CH_2CH_3$), 1.8 (br s, 3H, Me in isopropenyl), 2.7 (dd, J = 9, 14 Hz, 1H, 4-H_AH_B), 3.1 (dd, J = 11, 14 Hz, 1H, 4-H_AH_B), 4.2 (q, J = 7.0 Hz, 2H, -$CO_2CH_2CH_3$), 4.8 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (dd, J = 9, 11 Hz, 1H, 5-H_X), 6.2 ppm (br s, 1H, OH); mass 240 (M^+), 211 (M^+-Et), 167 (M^+-CO_2Et).

Anal. Calcd. for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.75; H, 8.24.

With Equimolar MeMgBr at Room Temp.

Under an argon atmosphere, to a solution of **4** (273 mg, 1.09 mmol) in dry diethyl ether (5 ml) was added 0.7 *M* methylmagnesium bromide diethyl ether solution (1.41 ml, 0.99 mmol), and the mixture was stirred at room temperature for 1 hour. After treating with saturated aqueous ammonium chloride solution, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was chromatogramed on a silica-gel column. Starting diester **4** (35 mg, 13%) was recovered as the fractions eluted with hexane-ethyl acetate (95:5). Ethyl 2-(1-hydroxy-1-methyl-ethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate **1c'** (104 mg, 40%, revised 46%) was obtained as the fractions eluted with hexane-ethyl acetate (98:2).

With Equimolar MeMgBr at –10°C.

Under cooling at –10°C, to a solution of **4** (511 mg, 2.01 mmol) in dry diethyl ether (5 ml) was added 0.7 *M* methylmagnesium bromide diethyl ether solution (2.80 ml, 1.96 mmol), and the mixture was stirred at –10°C for 1 hour. After treating with saturated aqueous ammonium chloride solution, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was chromatogramed on a silica-gel column eluting with with hexane-ethyl acetate (95:5) to give ethyl 2-(1-hydroxy-1-methylethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1c'**) (214 mg, 44%) and ethyl 2-acetyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**6**) (99 mg, 22%).

Ethyl 2-acetyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**6**), bp *ca.* 100 °C (6 mmHg)(bath temperature); ir (liquid flim): 1749 (COMe), 1709 cm^{-1} (CO_2Et); ^{1}H nmr ($CDCl_3$): δ 1.3 (*t*, J = 7.0 Hz, 3H, -$CO_2CH_2CH_3$), 1.8 (br s, 3H, Me in isopropenyl), 2.5 (s, 3H, COMe), 2.8 (dd, J = 9.0, 15.7 Hz, 1H, 4-H_AH_B), 3.2 (dd, J = 10.7, 15.7 Hz, 1H, 4-H_AH_B), 4.2 (q, J = 7.0 Hz, 2H, -$CO_2CH_2CH_3$), 4.8 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.3 ppm (dd, J = 9,0, 10.7 Hz, 1H, 5-H_X); mass 234 (M^+), 205 (M^+-Et), 161 (M^+-CO_2Et).

Anal. Calcd. for $C_{12}H_{26}O_4$: C, 64.03; H, 7.27. Found: C, 64.27; H, 7.19.

With Equimolar MeMgBr in Hexane-Diethyl Ether at –10°C.

Under cooling at –10°C, to a solution of **4** (510 mg, 2.01 mmol) in dry hexane (20 ml) was added 0.9 *M* methylmagnesium bromide diethyl ether solution (2.25 ml, 2.00 mmol), and the mixture was stirred at –10°C for 5 min. After treating with saturated aqueous ammonium chloride solution, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was chromatogramed on a silica-gel column eluting with hexane-ethyl acetate (95:5) to give ethyl 2-acetyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**6**) (172 mg, 38%), **1c'** (167 mg, 35%), 3,3,6-trimethyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**3c**) (10 mg, 3%), and ethoxy-3,6-dimethyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**8**) (5 mg, 1%).

3,3,6-Trimethyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**3c**); ir (liquid flim): 1748 cm^{-1} (lactone CO); ^{1}H nmr ($CDCl_3$): δ 1.4 (s, 6H, two Me), 1.9 (d, J = 1.5 Hz, 3H, 6-Me), 3.0 (dd, J = 1.5, 5.9 Hz, 2H, 8-H), 4.7 (s, 2H, 5-H), 6.0 ppm (dt, J = 1.5, 5.9 Hz, 1H, 7-H);); ^{13}C nmr ($CDCl_3$): δ 20.8 (6-Me), 23.4 (8-C), 24.3 (2C, 3-Me), 67.8 (3-C), 72.5 (5-C), 98.3 (8a-C), 130.4 (7-C), 133.7 (6-C), 172.6 (3a-C), 180.0 ppm (1-C).mass 194 (M^+).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 67.63; H, 7.4. Found: C, 68.02; H, 7.27.

3-Ethoxy-3,6-dimethyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**8**); ir (liquid flim): 1762 cm^{-1} (lactone CO); ^{1}H nmr ($CDCl_3$): δ 1.2 (t, J = 7.0 Hz, 3H, -OCH_2CH_3), 1.6 (s, 3H, 3-Me), 1.9 (dt, J = 1.5 Hz, 3H, 6-Me), 3.0 (dq, J = 1.5, 5.9 Hz, 2H, 8-H), 3.2-3.6 (m, 2H, -OCH_2CH_3), 4.7 (s, 2H, 5-H), 6.0 ppm (tq, J = 1.5, 5.9 Hz, 1H, 7-H); ^{13}C nmr ($CDCl_3$): δ 15.0 (-OCH_2CH_3), 20.5 (8-C), 22.7 (3-Me), 23.4 (6-Me), 59.2 (-OCH_2CH_3), 72.3 (5-C), 102.1 (3-C), 103.4 (8a-C), 130.1 (7-C), 133.9 (6-C), 170.7 (3a-C), 172.6 ppm (1-C), mass 224 (M^+), 179 (M^+-CO_2Et).

Reduction of 2-Acetyl-3-carboxylate **6** with $NaBH_4$)

To a solution of **6** (763 mg, 3.40 mmol) in ethanol (10 ml) was added sodium borohydride (38 mg, 1.0 mmol), and the mixture was stirred at room temperature for 30 min. After dilution with water, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was purified on a silica-gel column to give ethyl 2-(1-hydroxyethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1b'**) (398 mg, 52%) as the fractions eluted with hexane-ethyl acetate (90:10).

Ethyl 2-(1-Hydroxyethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylate (**1b'**), bp *ca*. 150-160 °C (6 mmHg)(bath temperature); ir (liquid flim): 3437 (OH), 1698 cm^{-1} (CO_2Et); ^1H nmr ($CDCl_3$): δ 1.3 (*t*, J = 7.0 Hz, 3H, -$CO_2CH_2CH_3$), 1.4 (d, J = 6.5 Hz, 3H, -$CO_2CH_2CH_3$), 1.7 (br s, 3H, Me in isopropenyl), 2.7 (dd, J = 8.3, 14.8 Hz, 1H, 4-H_AH_B), 3.1 (dd, J = 11.0, 14.8 Hz, 1H, 4-H_AH_B), 4.2 (q, J = 7.0 Hz, 2H, -$CO_2CH_2CH_3$), 4.7 (q, J = 6.5 Hz, 2H, -$CO_2CH_2CH_3$), 4.9 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.2 ppm (dd, J = 8.3, 11.0 Hz, 1H, 5-H_X).

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.43; H, 8.08.

General Procedure of Alkaline Hydrolyses of **1a', b', c'**)

A mixture of **1a', b', c'** (0.20 mmol) and 1.4% aqueous sodium hydroxide solution (0.87 g, 0.30 mmol) was stirred at room temperature for 24 h. After dilution with water, the mixture was washed with diethyl ether. The alkaline aqueous layer was collected, acidified with 10% hydrochloric acid, and extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The oily residue was purified on a silica-gel column to give corresponding hydroxyl acids **1a, b, c**.

2-(1-Hydroxymethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylic Acid (**1a**), colorless needles, 44%, as the fractions eluted with hexane-ethyl acetate (50:50), mp. 87-89.5 °C; ir (KBr disc): 3600-2400 (OH), 1668 cm^{-1} (CO_2H); ^1H nmr ($CDCl_3$): δ 1.8 (br s, 3H, Me in isopropenyl), 2.8 (dd, J = 8.8, 14.7 Hz, 1H, 4-H_AH_B), 3.1 (dd, J = 10.5, 14.7 Hz, 1H, 4-H_AH_B), 4.2-5.5 (br, 1H, -OH), 4.5 (br s, 2H, -CH_2OH), 4.9 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.2 ppm (dd, J = 9.0, 10.8 Hz, 1H, 5-H_X).

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.58; H, 6.66.

2-(1-Hydroxyethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylic Acid (**1b**), colorless oil, 52%, as the fractions eluted with hexane-ethyl acetate (80:20); ir (liquid flim): 3600-2400 (OH), 1668 cm^{-1} (CO_2H); ^1H nmr ($CDCl_3$): δ 1.5 (d, J = 6.5 Hz, 3H, -CH-CH_3), 1.8 (br s, 3H, Me in isopropenyl), 2.8 (dd, J = 8.3, 14.8 Hz, 1H, 4-H_AH_B), 3.1 (dd, J = 10.5, 14.8 Hz, 1H, 4-H_AH_B), 4.7 (q, J = 6.5 Hz, -CH-CH_3), 4.9 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.2 ppm (dd, J = 8.3, 10.5 Hz, 1H, 5-H_X).

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.40; H, 7.35.

2-(1-Hydroxy-1-methylethyl)-5-isopropenyl-4,5-dihydrofuran-3-carboxylic Acid (**1c**), colorless needles, 70%, as the fractions eluted with hexane-ethyl acetate (75:25), mp. 99-101 °C; ir (KBr disc): 3600-2400 (OH), 1668 cm^{-1} (CO_2H); ^1H nmr ($CDCl_3$): δ 1.5 (s, 6H, -CH_3), 1.7 (br s, 3H, Me in isopropenyl), 2.8 (dd, J = 9.0, 14.6 Hz, 1H, 4-H_AH_B), 3.1 (dd, J = 10.8, 14.6 Hz, 1H, 4-H_AH_B), 4.9 (br s, 1H, C=CH_AH_B in isopropenyl), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.2 (dd, J = 9.0, 10.8 Hz, 1H, 5-H_X), 6.5-7.2 ppm (br, 2H, -OH).

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.51; H, 7.69.

General Procedure of Lactonization of **1a,b,c** with Dicyclohexylcarbodiimide)

To a solution of **1a,b,c** (0.60 mmol) in dry benzene (5 mL) was added dicyclohexylcarbodiimide (126 mg, 0.61 mmol) and the mixture was stirred at room temperature for 30 min. After dilution with dry benzene, the filtrate was concentrated *in vacuo*. The oily residue was purified on a silica-gel column to give corresponding furolactone **2a,b,c**.

2-Isopropenyl-3,6-dihydro-4(2*H*)-furo[3,4-*b*]furanone (**2a**), colorless oil, 44%, as the fractions eluted with hexane-ethyl acetate (75:25), ir (liquid film): 1770 cm^{-1} (CO in lactone); ^1H nmr ($CDCl_3$): δ 1.8 (br s, 3H, Me in isopropenyl), 2.7 (tdd, J = 1.8, 8.2, 14.4 Hz, 1H, 3-H_AH_B), 3.0 (dd, J = 1.8, 9.8, 14.4 Hz, 1H, 3-H_AH_B), 4.7 (t, J = 1.8 Hz, 2H, 6-CH_2), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.1 (br s, 1H, C=CH_AH_B in isopropenyl), 5.9 ppm (dd, J = 8.2, 9.8 Hz, 1H, 2-H_X); ^{13}C nmr ($CDCl_3$): δ 16.7 (*C*H_3 in isopropenyl), 63.9 (6-C), 100.5 (5-C), 107.3 (6a-C), 114.2 (=*C*H_2 in isopropenyl), 141.5 (*C*=CH_2 in isopropenyl), 167.8 (3a-C), 186.4 ppm (1-C).

2-Isopropenyl-6-methyl-3,6-dihydro-4(2*H*)-furo[3,4-*b*]furanone (**2b**), colorless oil, 63%, as the fractions eluted with hexane-ethyl acetate (75:25), ir (liquid film): 1765 cm^{-1} (CO in lactone); ^1H nmr ($CDCl_3$): δ 1.5 (d, J = 6.7 Hz, 3H, 6-CH_3), 1.8 (br s, 3H, Me in isopropenyl), 2.7 (dd, J = 8.3, 14.3 Hz, 1H, 3-H_AH_B), 3.0 (dd, J = 9.8, 14.3 Hz, 1H, 3-H_AH_B), 4.8 (q, 1H, 6-H), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.1 (br s, 1H, C=CH_AH_B in isopropenyl), 5.8 ppm (dd, J = 8.3, 9.8 Hz, 1H, 2-H_X); ^{13}C nmr ($CDCl_3$): δ 16.4 and 16.7 (*C*H_3 in isopropenyl), 17.57 and 17.62 (3-C), 71.65 and 71.68 (3-C), 100.0 and 100.4 (5-C), 106.48 and 106.55 (6a-C), 114.0 and 114.1 (=*C*H_2 in isopropenyl), 141.66 and 141.70 (*C*=CH_2 in isopropenyl), 167.15 (3a-C), 189.6 ppm (1-C).

2-Isopropenyl-6,6-dimethyl-3,6-dihydro-4(2*H*)-furo[3,4-*b*]-furanone (**2c**), colorless oil, 84%, as the fractions eluted with benzene, ir (liquid film): 1762 cm^{-1} (CO in lactone); ^1H nmr ($CDCl_3$): δ 1.5 (s, 6H, 6-CH_3), 1.8 (br s, 3H, Me in isopropenyl), 2.7 (dd, J = 7.5, 14.2 Hz, 1H, 3-H_AH_B), 3.0 (dd, J = 9.8, 14.2 Hz, 1H, 3-H_AH_B), 5.0 (br s, 1H, C=CH_AH_B in isopropenyl), 5.1 (br s, 1H, C=CH_AH_B in isopropenyl), 5.8 ppm (dd, J = 7.5, 9.8 Hz, 1H, 2-H_X)); ^{13}C nmr ($CDCl_3$): δ 16.3 (*C*H_3 in isopropenyl), 24.0 and 24.2 (3-Me), 79.0 (3-C), 100.0 (5-C), 105.1 (6a-C), 114.0 (=*C*H_2 in isopropenyl), 141.9 (*C*=CH_2 in isopropenyl), 166.6 (3a-C), 191.9 ppm (1-C).

General Procedure for Thermal Ring-expansion of **2a,b,c**.

Furolactone **2a,b** (0.05 mmol) was heated at 100 °C for 1 hour. After cooling, the residue was purified on a silica-gel column to give corresponding oxepinolactone **3a,b**, but the starting material **2c** was recovered in this condition. So, furolactone **2c** (0.05 mmol) was heated at 120 °C for 30 min. After cooling, the residue was purified on a silica-gel column to give corresponding oxepinolactone **3c**.

3-Methyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**3a**), colorless oil, 44%, as the fractions eluted with benzene, bp ca 155-165 °C (8 mmHg)(bath temperature), ir (liquid film): 1755 cm^{-1} (CO in lactone); ^1H nmr ($CDCl_3$): δ 1.9 (d, J = 1.5 Hz, 3H, 6-Me), 3.0 (br d, J = 5.9 Hz, 2H, 8-H_2), 4.5 (t, J = 1.5 Hz, 3-H_2), 4.7 (s, 2H, 5-H_2), 6.0 ppm (t, J = 1.8, 5.9 Hz, 1H, 7-H); ^{13}C nmr ($CDCl_3$): δ 20.9 (8-C), 23.3 (6-Me), 66.7 (3-C), 72.3 (5-C), 100.5 (8a-C), 130.4 (7-C), 133.8 (6-C), 174.2 (3a-C), 174.3 ppm (1-C).

3,6-Dimethyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**3b**), colorless oil, 44%, as the fractions eluted with benzene, bp ca 140-160 °C (7 mmHg)(bath temperature), ir (liquid film): 1755

cm^{-1} (CO in lactone); ^1H nmr ($CDCl_3$): δ 1.4 (d, J = 6.6 Hz, 3H, 3-Me), 1.9 (d, J = 1.8 Hz, 3H, 6-Me), 3.0 (br d, J = 5.9 Hz, 2H, 8-H_2), 4.7 (q, J = 6.6 Hz, 3-H_2), 4.7 (s, 2H, 5-H_2), 6.0 ppm (t, J = 1.8, 5.9 Hz, 1H, 7-H); ^{13}C nmr ($CDCl_3$): δ 17.6 (3-Me), 20.8 (8-C), 23.3 (6-Me), 72.3 (3-C), 74.1 (5-C), 99.7 (8a-C), 130.4 (7-C), 133.8 (6-C), 173.4 (3a-C), 177.3 ppm (1-C).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.38; H, 6.77.

3,3,6-Trimethyl-5,8-dihydro-1(3*H*)-furo[3,4-*b*]oxepinone (**3c**), colorless needles, 63%, as the fractions eluted with hexane-ethylacetate (95:5), bp ca 120-140 °C (8 mmHg)(bath temperature), mp 71-73 °C, ir (KBr disc): 1748 cm^{-1} (CO in lactone); ^1H nmr ($CDCl_3$): δ 1.4 (s, 6H, 3-Me), 1.9 (d, J = 1.5 Hz, 3H, 3-Me), 3.0 (dd, J = 1.5, 5.9 Hz, 2H, 8-H_2), 4.7 (s, 1H, 5-H_2), 6.0 ppm (dt, J = 1.5, 5.9 Hz, 1H, 7-H); ^{13}C nmr ($CDCl_3$): δ 20.8 (8-C), 23.4 (6-Me), 24.3 (3-Me), 67.8 (3-C), 72.5 (5-C), 98.3 (8a-C), 130.4 (7-C), 133.7 (6-C), 172.6 (3a-C), 180.0 ppm (1-C).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.63; H, 7.42.

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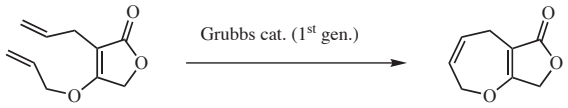

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